

CA20N
Z 1
-83H021



3 1761 11849828 6



Ontario

64

MacLEOD (cont'd)

ROYAL COMMISSION OF INQUIRY INTO CERTAIN
DEATHS AT THE HOSPITAL FOR SICK CHILDREN AND
RELATED MATTERS.

In ch. PMR (cont'd)

Hearing held
8th floor
180 Dundas Street West
Toronto, Ontario

Shumiehofer
Roland

The Honourable Mr. Justice S.G.M. Grange

Commissioner

P.S.A. Lamek, Q.C.

Counsel

E.A. Cronk

Associate Counsel

Thomas Millar

Administrator

Fordlin

Transcript of evidence
for

Hunt

November 10, 1983.

Knarman

VOLUME 64

Olak

OFFICIAL COURT REPORTERS

Angus, Stonehouse & Co. Ltd.,
14 Carlton Street, 7th Floor,
Toronto, Ontario M5B 1J2

595-1065



ROYAL COMMISSION OF INQUIRY INTO CERTAIN
DEATHS AT THE HOSPITAL FOR SICK CHILDREN
AND RELATED MATTERS.

Hearing held on the 8th Floor,
180 Dundas Street West, Toronto,
Ontario, on Thursday, the 10th
day of November, 1983.

- - - - -

THE HONOURABLE MR. JUSTICE S.G.M. GRANGE - Commissioner
THOMAS MILLAR - Administrator
MURRAY R. ELLIOT - Registrar

- - - - -

APPEARANCES:


P.S.A. LAMEK, Q.C.)	Commission Counsel
E. CRONK)	
T. C. MARSHALL, Q.C.)	Counsel for the Attorney
D. HUNT)	General and Solicitor General
L. CECCHETTO)	of Ontario (Crown Attorneys
	and Coroner's Office)
I. J. ROLAND)	Counsel for The Hospital for
R. BATTY)	Sick Children
B. PERCIVAL, Q.C.)	Counsel for The Metropolitan
D. YOUNG)	Toronto Police
W. N. ORTVED	Counsel for numerous Doctors
	at The Hospital for Sick
	Children
F. KITELY	Counsel for the Registered
	Nurses' Association of Ontario
	and 35 Registered Nurses at
	The Hosiptal for Sick Children

(Cont'd)



APPEARANCES: (Continued)

J. SOPINKA, Q.C.)	Counsel for Susan Nelles -
D. BROWN)	Nurse
E. FORSTER	Counsel for Phyllis Trayner -
	Nurse
J. A. OLAH	Counsel for Janet Brownless -
	R.N.A.
B. KNAZAN	Counsel for Mrs. M. Christie -
	R.N.A.
S. LABOW	Counsel for Mr. & Mrs. Gosselin,
	Mr. & Mrs. Gionas, Mr. & Mrs.
	Inwood, Mr. & Mrs. Turner and
	Mr. & Mrs. Lutes (parents of
	deceased children)
F. J. SHANAHAN	Counsel for Mr. & Mrs. Dominic
	Lombardo (parents of deceased
	child Stephanie Lombardo); and
	Heather Dawson (mother of
	deceased child Amber Dawson)
W. W. TOBIAS	Counsel for Mr. & Mrs. Hines
	(parents of deceased child
	Jordan Hines)
J. SHINEHOFT	Counsel for Lorie Pacsai and
	Kevin Garnet (parents of
	deceased child Kevin Pacsai)



Digitized by the Internet Archive
in 2024 with funding from
University of Toronto

<https://archive.org/details/31761118498286>



INDEX OF WITNESSES

<u>NAME</u>	<u>Page No.</u>
MacLEOD, (Dr.) Stuart Maxwell; Resumed	4226
Direct Examination by Mr. Lamek (Cont'd)	4233
Cross-Examination by Mr. Shinehoft	4285
Examination by Mr. Roland	4307
Cross-Examination by Mr. Brown	4343
Cross-Examination by Ms. Forster	4347
Cross-Examination by Mr. Hunt	4376
Cross-Examination by Mr. Knazan	4406
Cross-Examination by Mr. Olah	4426

INDEX OF EXHIBITS

<u>No.</u>	<u>Description</u>	<u>Page No.</u>
255	Study of Unit Dose Drug Distribution in Four Canadian Hospitals, produced by Dr. MacLeod.	4307
256	Paper entitled: Progesterone Derivatives that Bind to the Digitalis Receptor, published by The American Society for Pharmacology in Molecular Pharmacology.	4308



--- on resuming at 10:00 a.m.

STUART MAXWELL MacLEOD, Resumed

THE COMMISSIONER: We are running into all kinds of scheduling problems and I want to discuss them with you so that we can see what can be done.

First of all, do you want to tell us about the witness problems for next week?

MR. LAMEK: Mr. Commissioner, the witness problem for next week is easily stated. There is no witness for next week. By way of explanation of that - Dr. MacLeod, who, if ~~we~~ ^{he} were to finish with him at noon today, we would probably not have completed his evidence, and he is not available next week; he is out of town.

We are coming to that stage of the Inquiry where we are looking to the out-of-town professionals. It has been difficult to give them a clear date well in advance of their appearance because it has been difficult to predict just when we would reach them. Professional people are just not available on short notice. We do have witnesses for the weeks of the 21st, the 28th and whatever the ~~third~~ ^{first} week in December is, but next week, we do not have a witness.

THE COMMISSIONER: Can you tell us what they are now?



1 MR. LAMEK: Yes.

2 Dr. Fay or Dr. Hastreiter, one
3 or the other, will be here the week of the 21st;
4 Dr. Kauffman, the week of the 28th, and the following
5 week, Dr. Merkin, and they will be followed by the
6 authors of the Atlanta Report.

7 THE COMMISSIONER: Yes. All right.

8 Now, here is the problem. We
9 scheduled the argument for this afternoon on two
10 matters, the other argument, the other two matters,
11 and I am hoping to get the papers in today, the reply
12 papers, and the thought occurred to me that it might
13 be advisable to allow me to mull over the two
14 written problems; namely, naming of names and the
15 scope of the police inquiry, and give judgment on that
16 sometime early next week - Monday will not be possible
17 but Tuesday is quite possible - and reserving on
18 the other two matters until after that has happened.

19 Several counsel have mentioned to
20 me that much of the argument on the oral matters;
21 namely, the notice under Section 5 and the production
22 of the police report, would depend upon the answers
23 to the other questions.

24 If that were satisfactory, we would
25 adjourn this afternoon's argument and try to fit it
in sometime on Tuesday. I don't know whether that is



1

2

possible. This will make no difference to the meeting this afternoon, Mr. Brown, in any event, but it might solve the police report problem by that meeting.

5

6

What do you have to say, Mr. Shinehoft.

7

8

MR. SHINEHOFT: Mr. Commissioner, I understand that you intend then to continue with the examination of this witness this afternoon?

9

10

THE COMMISSIONER: That was the thought, because we can't have him next week and we can't fit him in after that.

11

12

13

MR. SHINEHOFT: My problem is this, Mr. Commissioner, just speaking for myself, I had assumed that this afternoon there was going to be oral argument...

14

15

16

THE COMMISSIONER: I know, and you made other arrangements.

17

18

19

MR. SHINEHOFT: ...and did not intend to be here for the oral argument, and I have therefore made other arrangements for this afternoon.

20

21

THE COMMISSIONER: The problem, you see, Mr. Shinehoft, you have to accept that if we have to satisfy everybody, it becomes insolvable; I don't know how we do it.

22

23

24

25



1

2

3

4

5

6

7

8

9

10

11

12

13

14

15

16

17

18

19

20

21

22

23

24

25

MR. SHINEHOFT: One possibility, if the witness is not going to be finished today and will have to be brought back, is that I can examine then, or perhaps if I could examine prior to other people examining.

THE COMMISSIONER: I don't see any reason why that couldn't be done this morning, because Mr. Lamek tells me he will be finished.

I don't know, has anyone any objection to Mr. Shinehoft going first, after Mr. Roland?

MR. ROLAND: I am quite happy to cede my place to Mr. Shinehoft. I don't think there is any magic in going next.

THE COMMISSIONER: All right.

MR. ROLAND: We started on this procedure early on but, you know, I am prepared to do that.

THE COMMISSIONER: Well, either way, then, we will fit you in this morning.

MR. SHINEHOFT: Thank you very much, Mr. Commissioner.

THE COMMISSIONER: There is nobody else here to complain, apparently, so that will help out no end.

MR. SHINEHOFT: It may be that they



1

2

are so concerned about the nature of the questions
I am going to ask this witness that they really don't
have any complaints to make!

4

5

THE COMMISSIONER: Any other
comments?

6

7

MR. BROWN: Speaking with respect
to the adjournment of the oral argument --

8

THE COMMISSIONER: Yes.

9

10

MR. BROWN: -- having arranged to
have everyone together in one place, I certainly
prefer, at this point, to go with certainty rather
than uncertainty and rescheduling it for sometime
next week. I have no idea of the schedule of Mr.
Sopinka or Mr. Percival.

11

12

13

14

15

16

17

18

19

20

21

22

23

24

25

THE COMMISSIONER: Well, we will
be able to talk to them this afternoon; they will be
here. We can see what the situation is, but I am
just suggesting Tuesday as the date upon which I
can give judgment on the matters on which I have
received written argument. We will proceed with the
oral argument after that. And if they tell us
they can't proceed with their oral argument after that,
then we can't; we may have solved the police report
problem by then by agreement and the only one will be
the notice question. That is not that urgent.



1

2

MR. BROWN: No. I agree.

3

4

5

6

7

Can we still leave open the possibility, however, if we are not able to reach an agreement this afternoon that, if next week is not available to those people, we can have the argument on the police report this afternoon?

8

9

10

THE COMMISSIONER: Well, I don't think you can leave it open because Dr. MacLeod has now made other arrangements.

11

12

How did you make out?

13

14

15

16

17

18

THE WITNESS: Well, I cancelled my clinic for this afternoon.

19

20

21

22

23

24

25

THE COMMISSIONER: Yes. All right.

So, I think we will call that off this afternoon, in any event, except we will not call off the meeting because I would like to have that meeting and it will only take about ten minutes.

And, Miss Forster, you are invited to this meeting as well.

MS. FORSTER: Thank you, sir.

THE COMMISSIONER: And you, Mr. Percival, and Mr. Sopinka, if he is available.

All right.

MR. SHINEHOFT: One other matter.

I take it, Mr. Commissioner, we are



1
2 not sitting on Monday and that we will be coming
3 here on Tuesday?

4 THE COMMISSIONER: I think we are
5 not sitting here on Monday. I think that is
6 established, because we have no witness. I will
7 probably give judgment right here on Tuesday on the
8 matter. Nobody has to appear for that if they don't
9 want to.

10 MR. SHINEHOFT: Thank you.

11 THE COMMISSIONER: It is a place
12 to give it, and that is what I intend to do at ten
13 o'clock on Tuesday, unless we notify you to the
14 contrary. I hope that I will watch my step a bit
15 more carefully this weekend than last. That is the
16 only thing that might happen.

17 MS. FORSTER: Excuse me, Mr.
18 Commissioner. Have I got my dates mixed up or is
19 it next week we were supposed to be in the Court House?

20 THE COMMISSIONER: Yes. And we are
21 not going to be there.

22 What was happening was that they
23 needed this place for Wednesday and Thursday of next
24 week and they told us, if we wanted to have a court-
25 room, we had to go there on Monday. So, we are not
going to go on Monday. We are not going to bother with



1
2 the whole thing. Tuesday is the only day we will
3 be sitting here next week.

4 MS. FORSTER: Thank you, sir.

5 THE COMMISSIONER: You may hear to
6 the contrary, if I am not able to give that judgment.

7 Now, Mr. Millar, could you settle
8 that matter with the Court House then?

9 MR. MILLAR: Yes, I will, sir.

10 THE COMMISSIONER: All right.
11 Thank you.

12 MR. MILLAR: Thank you very much.

13 THE COMMISSIONER: Mr. Lamek, will
14 you proceed.

15 MR. LAMEK: Yes. Thank you, sir.

16 DIRECT EXAMINATION BY MR. LAMEK (Continued):

17 Q. Dr. MacLeod, we talked
18 yesterday at the end of the day about the case of
19 Kristin Inwood. Can we move now to the case of
20 Kevin Pacsai, and perhaps the Registrar would be
21 good enough to give you the chart in case you want to
22 refer to it.

23 I take it, doctor, you are familiar
24 with the child's hospital course?

25 A. Yes, I am.

Q. And with his history in



1

2

Hamil-ton before his transfer to the Hospital for
Sick Children?

3

4

A. In a general outline, at
any rate.

5

6

Q. And the incidents there
of elevated potassium, acidosis, arrhythmias, shock,
CHF and so on?

7

8

A. Yes, I am familiar with
that. Yes.

9

10

Q. And you are aware, I take
it from your review of this chart, that when Dr.
Costigan saw this child in the middle of the night
and the early morning hours of March 12, 1981, he
was concerned about the arrhythmias and the heart
blood that he was seeing at that time and made a
differential diagnosis on the chart of sick sinus
syndrome or digoxin intoxication; he queried both
those possibilities?

11

12

13

14

15

16

17

18

A. Can you tell me which page
that is on? I do recall reading it.

19

20

Q. Sure. That is at page 63,
I believe - yes, page 63. It is made at 5:30 in
the morning by Dr. Costigan. He took off the
rhythm strip from the monitor on the child; found
slightly PR interval, some bradycardia;

21

22

23

24

25



1

2

sinus or nodal tachycardia, intermittent, ²⁵¹~~221~~ heart
blood, and made a differential diagnosis, sick
sinus or digoxin toxicity.

4

5

A. Yes, I see that.

6

7

8

Q. And I take it, doctor, in
light of the observations that he records there,
you would not think those to be unreasonable dif-
ferential diagnoses?

9

10

11

12

A. Well, I might quibble with
the diagnoses, but it is -- this is not what I would
normally call a sick sinus syndrome, but the
description above is correct.

13

14

15

16

17

18

19

20

21

22

23

24

25



DP.jc
B

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25

Q Do I take it from that answer, Doctor, that you would not quarrel with his raising the possibility of digoxin toxicity?

A No, I think that is a reasonable differential diagnosis.

Q And he made the same differential diagnosis on the child's admission to the I.C.U., half an hour to one hour later. That is on page 66.

A Yes.

Q Now, you see at the bottom of page 66 that there was a repeat calcium level ordered. He had sent down a sample for electrolytes and the sample had come back with the report, calcium 9-point-something, but hemolyzed.

A Potassium, I think it is.

Q Sorry, potassium, but a hemolyzed sample, drew another and sent it down for immediate analysis and received a level of 7.7 potassium.

A Yes.

Q As you know, Doctor, it was subsequently discovered that this child had an ante mortem serum digoxin level of greater than 10 nanograms per millilitre and a post mortem digoxin level of 25-26 nanograms. His ante mortem level of digoxin



B.2

1

2

on arrival at the Hospital had been 1.8 nanograms
per millilitre. He had been digitalized in Hamilton.

4

A. Yes.

5

6

7

8

9

10

Q. And to fill out the digoxin
information picture, levels have been recorded in
fixed heart and lung tissues ~~and~~ subject to severe
difficulties in interpretation, as we have heard
about often; and are you aware that a post mortem blood
sample was sent to Mount Sinai for assay and was
returned with a level of 112 nanograms per millilitre?

11

A. Yes, I have heard that.

12

13

Q. Do you regard that as a reliable
assay result?

14

15

16

17

A. I have no basis on which to
judge whether it is reliable or not reliable. I think
it has to be seen as being in conflict with at least
two measurements made in other laboratories that are
at variance, so I guess it is two against one.

18

19

20

21

22

Q. Certainly, you are quite right.
There was an assay done at the Centre of Forensic
Sciences which produced a level of 26 I believe it was,
which was entirely consistent with the Hospital's
own assay result.

23

24

25

A. And in fairness I think that
the clinical course which I guess you are coming to



B.3

1

2

is more compatible with the lower reading than the
higher.

3

4

Q. 112?

5

A. Yes.

6

7

Q. Certainly whatever it may mean,
the 112 nanograms assay result is there but it does
rather stick out of the profile of the other digoxin
results. I guess we can say no more than it is
another, but perhaps anomalous.

8

9

10

11

12

13

14

15

16

17

18

19

20

21

22

23

24

25

A. I think the judgment of those
at the Hospital who reviewed these data ad nauseam
over the last year and a half, our judgment has been
that that probably was laboratory error, probably a
dilution mistake, the kind of thing which is fairly
commonly made in laboratories.

Q. Doctor, do you have an opinion
as to whether one can reasonably infer from the
recorded levels of greater than 10 and 25 that this
child received an unprescribed or unrecorded dose
of digoxin?

A. I think as usual there is a
spectrum ranging from possible to probable, and some-
where within that spectrum I think you can conclude
that this child probably had an extra dose of digoxin.

Q. Dr. Spielberg has suggested



B.4

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25

that the level may have been caused by the child's pathophysiological condition, that there may have been an unbinding of digoxin from tissue resulting from the child's condition.

Is that your understanding of the suggestion that Dr. Spielberg has made?

A. Yes, I think so. Certainly I would agree with that suggestion. I think it is a very distinct possibility in this particular child.

Q. What is there in this child's condition to which you would particularly point as providing a basis for regarding that as a perfectly plausible hypothesis?

A. I suppose the most striking thing is the abnormalities of potassium and acid base balance that were seen in Hamilton long before there was any question of digitalis toxicity and which reappeared again at the time of the agonal event. We know, and I am sure you have heard more than you want to hear about the relationship or interrelationship between potassium and digoxin, so a high potassium can certainly cause some digoxin release and an elevation of digoxin concentrations, and the reverse of course is true as well, as we discussed yesterday.



B.5

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25

That certainly would lead you to give serious consideration, I think, to the possibility that the primary abnormality here is one of potassium metabolism or of acid base metabolism. I don't think you could say that with any certainty, but it is certainly a distinct possibility.

Q. Let me go back for a moment. The two hypotheses I suppose so far for the explanation of the elevated digoxin levels first are, one, the possibility of an unprescribed or unrecorded dose or, two, an elevation in serum as a result of physiological changes in the child and some unbinding which may reflect the presence of the high potassium. Is that fair? Have I correctly stated that?

A. Yes, those are I think the two --

Q. The two prime candidates?

A. Yes, two possible explanations.

Q. As between those two, is there really anything to choose between them, Doctor, or is that really a flip of the coin? I ask it in that way because I understand what you have said, we don't know whether the potassium was high because digoxin was high; if it were, that would argue for the unprescribed dose or we don't know whether the digoxin was high because the potassium was



B.6

1

2

high, which would argue in favour of the patho-
physiology argument, would it not?

4

A. Yes.

5

Q. Is it really any more than a
coin flip on this one?

6

7

8

9

10

A. I think you could find a
break point in the spectrum from possibility to
probability which would be a consensus, and I don't
think it would be 50/50, but I am not sure I want
to name you a figure.

11

12

Q. On which side do you fall with
respect to those two contenders for the explanation?

13

14

A. I would say probably 75 per
cent leaning towards the extra dose of digoxin, 25 per
cent on the pathophysiology.

15

16

17

Q. But there has to be a substantial
question in your mind, in making that preference, I
take it?

18

19

20

21

22

23

24

25

A. Oh, yes, but there is a very
real - the pathophysiology argument cannot be
discounted at all in this case and certainly became
stronger I think when we consider the Murphy inquest
in April-May - I guess the inquest was in May. The
events and conclusions that were reached at that
inquest really I think strengthened the belief that



B.7

1

2

possibly what we are seeing in Pacsai is some poorly understood pathophysiology leading to a high digoxin.

3

4

5

6

Q. Do you regard the physiological and clinical condition of Pacsai as comparable with that of Gary Murphy? Would it be of assistance to you to have the Gary Murphy chart?

7

8

9

10

11

12

13

14

15

16

17

18

A. Yes. I honestly have not read the clinical chart on Gary Murphy and I don't think you want to sit here while I read it. I believe Gary Murphy though had quite significant structural heart disease and Pacsai really did not. Pacsai's problems were not structural, i.e. they were conduction problems, difficulties in the conduction system which really, as I understand it, cannot be analyzed very well by histological or pathological analysis. So they are not really comparable in that sense, although both of them clearly could be said to have significant life threatening heart disease, generically, heart disease.

19

20

21

Q. What about the other aspects of their clinical conditions? Do you regard them as comparable?

22

23

24

25

A. I am really not in a position to talk about Murphy and I think probably I should just stay off of that.



B.8

- 1
- 2
- 3
- 4
- 5
- 6
- 7
- 8
- 9
- 10
- 11
- 12
- 13
- 14
- 15
- 16
- 17
- 18
- 19
- 20
- 21
- 22
- 23
- 24
- 25

Q. In terms of the pathophysiology hypothesis leading to unbinding of tissue and release into serum and so on, is that a function of the overall clinical picture of the child, or of the cardiac picture of the child?

-

-



C
BB/cr

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25

A. Well, I think it can be either. I don't think you can make a distinction at all since there are a number of factors such as potassium concentration or magnesium concentration or calcium concentration which are general phenomena occurring throughout the body which may influence the release or the binding of digoxin at various tissue sites.

Q. Yes.

A. There are presumably local factors in myocardium as well which may be similar but I am not sure I followed your question.

Q. Well, I guess what I am saying is this. Does one focus upon the cardiac condition of the child in considering the likelihood of unbinding as a result of pathophysiology?

A. No, I think not.

Q. One looks at the whole child and the whole of its system, one looks I take it for necrosis in all tissues which may have the effect of unbinding digoxin and that sort of thing?

A. Yes, absolutely. We know that only a small percentage of the total body digoxin load is actually bound in myocardial muscle. There is, relatively speaking, larger amounts found



1
2 in skeletal muscle, liver and kidney, skin, you
3 know, virtually every tissue. So, I think that it
4 would be a mistake to just focus on the pathological
5 events in the heart as an explanation. It may be
6 relevant, say, in a case like Miller where there is
7 distinct trauma to myocardium or a case like Murphy
8 I believe where there was some myocardial necrosis
9 so that breakdown of those myocardial muscle cells
10 and some release of digoxin on that basis. So, there
11 is a local phenomenon that causes an increase.
12 But it might equally well be necrosis in skeletal
13 muscle.

14 Q. Yes. Now, Dr. MacLeod,
15 if an unprescribed dose were given to Baby Pacsai
16 are you able to form an opinion from the chart and
17 from the recorded levels about when it was likely
18 administered and, in particular, let me ask you
19 this question. Could a dose prior to 3:45 in the
20 morning have produced the symptoms which led
21 eventually to the child's transfer to the ICU.
22 I am sorry, I said 3:45, prior to 5:30 in the
23 morning have produced those symptoms which were
24 recorded on page 63 and which led eventually to
25 the child's transfer to the ICU.

A. No, I am sorry, your question



1

2

as to time is at 5:30 or prior to 5:30?

3

4

5

Q. Prior to 5:30, the symptoms having been observed, certain symptoms having been observed at 5:30.

6

7

8

A. And the actual time on that sample, the initial digoxin measurement, potassium and digoxin was 600?

9

10

Q. I meant to say 6:30, 6 to 6:30. It was after he was in the ICU.

11

12

13

A. Yes. Well, prior to is a pretty vague word.

14

15

16

THE COMMISSIONER: I am sorry, one moment. One moment. Yes, Mr. Shinehoft.

17

18

19

20

MR. SHINEHOFT: I don't want to interrupt my friend but I assume, Mr. Lamek, that you are contemplating an IV administration of the drug as opposed to an oral administration?

21

22

23

24

25

MR. LAMEK: Well, I am not contemplating anything at the moment because that may be something that goes into this whole mix. I hope Dr. MacLeod may be able to tell us about that.

THE COMMISSIONER: Yes, all right.

THE WITNESS: Well, I think it is certainly possible that there was administration



1
2 prior to, anywhere from seconds to hours before
3 5:30.

4 Q. And again you say possible,
5 and I know it is a very vague and difficult question
6 to answer. The arrest in this child occurred at
7 approximately 8 o'clock in the morning.

8 MR. OLAH: Excuse me, Mr.
9 Commissioner, because this is a critical area in
10 terms of timing. I believe the chart shows that the
11 transfer took place some time after 6 o'clock.
12 You will see on page 65 there is a note on the ward
13 by Nurse Nelles from 3:45 in the morning to 6:00 a.m.
14 So, the transfer probably took place some time after
15 6 o'clock not at 5:30.

16 MR. KNAZAN: Mr. Commissioner,
17 Dr. Costigan testified that he wheeled him up
18 some time I think between 5:30 and a quarter to
19 six.

20 MR. LAMEK: I'm sorry, what happened
21 between 5:30 and a quarter to six?

22 MR. KNAZAN: I am agreeing with
23 you, Mr. Lamek. Dr. Costigan said ---

24 MR. LAMEK: I didn't hear you.

25 MR. KNAZAN: Couldn't put a time
on it. So, I think it is a matter from the evidence,



1
2 I don't think Mr. Olah is right that it was at
3 6 o'clock.

4 MR. LAMEK: Well, Mr. Commissioner,
5 what we do know, and the point that I was focussing
6 on for the moment without having the precise time
7 before me is that the arrest apparently occurred at
8 about 8:45 in the morning. That appears from page
9 67.

10 THE COMMISSIONER: Yes, all right.

11 MR. LAMEK: 0845 approximately,
12 the child became apneic, suffered bradycardia,
13 followed almost immediately by ventricular
14 fibrillations and they started administering bicarb
15 and so on without response, defibrillation occurred.
16 The arrest appears to have been 8:45 in the morning.
17 The transfer to the ICU, as I recall Dr. Costigan's
18 evidence, occurred at about 6 o'clock in the morning
19 and the sample was drawn shortly after the child's
20 admission to the ICU.

21 A. Yes.

22 MR. LAMEK: Is that right?

23 MS. CRONK: Yes.

24 MR. LAMEK: Q. Now, in terms of
25 attempting to find or attempting to identify a
range of time for the administration of the dose



1

2

3

4

5

if one were administered, Doctor, I take it it is important to recognize the time of the arrest, first of all, because we have to work back from that point, do we not, if the arrest is attributable to digoxin?

6

A. Yes, but I really fail to see how the time of arrest will be very helpful.

7

6

Q. Okay, why not?

8

9

10

11

A. Well, because this was clearly a kind of stuttering downhill course for this child that went on over three, more than three hours leading up to the arrest.

12

Q. Yes.

13

14

A. I mean, that is perfectly compatible with his disease or with the influence of digoxin.

15

Q. Okay.

16

17

A. With a gradual onset of progressively more severe toxicity.

18

19

20

21

22

23

24

25

Q. Okay. Well, that is really the question I was getting at because as I understood it certainly in the case of Cook the view of Dr. Spielberg has been, and I thought essentially, subject to some variation, yours was the same, that administration probably occurred not more than an hour or so before the actual death?



1

2

3

4

5

6

7

8

9

10

11

12

13

14

15

16

17

18

19

20

21

22

23

24

25

A. Well, I think that would be difficult to say in this particular case.

Q. Okay.

A. Again you could come up with a range from possible to probable but I think I could personally much more readily accept a long course even if it is digitalis toxicity that we are seeing here in this particular child.

Q. Okay, that is really what I am getting at.

A. Yes.

Q. That the possibility of administration prior to 5:30 in the morning is not necessarily eliminated by the fact that the terminal events didn't occur until a quarter to nine?

A. No, I would say not at all.

Q. All right. Now, in so saying, Dr. MacLeod, are you making any judgment as to the more likely route of administration of a dose prior to 5:30?

A. I don't think one wants to judge the route of administration here, I am just saying it is compatible with an earlier administration. I think it goes without saying that if the drug was administered prior to 5:30 it was almost



1

2

certainly administered orally.

3

Q. Okay.

4

A. I think it is very unlikely,

5

given the values that we have, that it was administered
intravenously prior to 5:30.

6

7

Q. I take it intravenous

8

administration prior to 5:30 -- no, no, forget that.

8

9

Forget that, I was leading myself down a path that
led nowhere.

10

Doctor, in light of the observations

11

that you have made about the child's course you

12

have described it as a sort of stuttering downhill

13

three hour course from 5:30 to 8:30, 8:45, is

14

there in your view a more likely time for

15

administration of a dose than prior to 5:30?

16

A. I am sorry, I am not sure

17

I follow you. Is it more likely prior to 5:30 than
later?

18

Q. Are you more likely prior

19

to or subsequent to 5:30, yes.

20

A. I think if a dose has been

21

administered it is more likely prior to 5:30.

22

Q. Dr. MacLeod, once again

23

just seeing how far I can take that. Are you able

24

to form any judgment as to an outside early time

25



1

2

for administration?

3

4

5

6

7

8

A. No, I think that would be very difficult. There clearly has to be - if you assume, and this I think is a big assumption, if you assume that these rhythm disturbances described at 5:30 were due to digoxin, if you assume that the elevation of potassium, this unequivocally measured at 6 o'clock or shortly, 6:15, say.

9

10

11

12

13

14

15

16

17

18

19

20

21

22

23

24

25

Q. Yes.

A. It doesn't really matter,

if you assume that those are due to digoxin and if you assume that the digoxin was given orally you really must allow time for absorption and onset of pharmacologic effect, i.e. interruption of the drug within pharmacologic receptor in the kidney and in other tissues and in the heart which would lead to these phenomena. It doesn't happen instantaneously and certainly not after an oral dose.

So, the kinds of figures we talked about yesterday would probably apply, that you have a lag time to peak concentration and a further lag time to peak effect.

- - - -



DM.jc
D

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25

A. Again it depends, when you talk about the effects, the biochemical effects, or the effects on the heart, it is really impossible to be very dogmatic because you don't know the absolute magnitude of the dose.

Q. Yes.

A. That is the real unknown here. But assuming that, you know, that this was not a particularly huge dose, it wouldn't have to be a huge dose to produce these numbers, particularly allowing for the post mortem multiplier effect. I mean, you could reasonably expect to see these concentrations with a dose of maybe 100 or 150 micrograms of digoxin given orally. If that is the case you are really talking about an administration of one to two hours prior to 5:30.

Q. Could you transcribe 100 to 150 micrograms in terms of vials paediatric or adult?

A. Well, we are talking about oral dosing there.

Q. Yes.

A. So that would be 3 mls of the paediatric elixir which has 50 micrograms per ml, 2 to 3 mls of that.

Q. Can you in fact administer the



D.2

1

2

parenteral preparation orally?

3

A. I don't see any reason why not.

4

I really am not certain as to how well absorbed it would be. The paediatric elixir is in an alcohol base and this is quite well absorbed because of that. I guess the parenteral one is too, as you have heard with the propylene glycol and some ethyl alcohol in there as well. So it probably would be absorbed in a very similar fashion to the elixir.

5

6

7

8

9

10

THE COMMISSIONER: I must be missing something, Doctor, you said would probably be orally, why could it not be an IV dose?

11

12

13

14

15

16

17

18

19

20

21

22

23

24

25

THE WITNESS: Well, I think - I would expect - I don't think you can rule out an IV dose absolutely. I perhaps was a little more forceful in the statement than I should have been. I would have expected with an intravenous dose that you would have seen a more calamitous downhill course than this. It is really the pattern of the death that influences me the most. If this was a slow progression over a three and a half - or four hours probably, and I think in a child with this kind of rhythm disturbance an intravenous administration which likely would have produced much higher levels. I mean, if you assume that the level was 10 at 6:15, or 10.6 at



D.3

1

2

3

4

5

6

7

8

9

10

11

12

13

14

6:15, then it must - when you get back, that will be well out beyond the alpha distribution phase, given the fact that the clinical events were noted at 5:30, the note is written at 5:30, so the clinical events were probably noted at 500 or earlier. So you are moving back and it takes you away from that alpha phase. So if you assume an intravenous administration was causing this, you are already into steady state and then you are talking about rather large concentrations being administered, and it becomes unlikely that survival, that the child would have survived given his pre-existing rhythm disturbance, would have survived for four hours after that.

15

There are a lot of assumptions, and certainly this is not a case that anybody would want to be dogmatic about, I can assure you.

16

17

Q All this on the assumption, Doctor, that indeed there was a dose administered?

18

19

A That is correct.

20

Q I want to be sure I understand. Your best judgment is, on that assumption, that the dose was probably prior to 5:30. Do I understand you to be saying that if the dose were administered intravenously it would likely be (a) not a huge dose;

21

22

23

24

25



D.4

1

2

and (b) not very much prior to 5:30?

3

A. I think the calculations change
if you are talking about an intravenous dose.

4

5

Q. Yes.

6

7

8

9

10

11

12

A. Then - I haven't done the
actual mathematics although I will do them if you
want. You would have to postulate some larger dose
intravenously, not necessarily larger than one adult
ampule. I think one adult ampule in ball park figures
would still account for a concentration of 10 or even
15 nanograms per ml at the time of death. So I am
working back from 26.

13

Q. Yes.

14

15

16

17

18

A. And saying, okay, there is
maybe a twofold multiplier, so perhaps the agonal
concentration was 13; and if you postulate other
normal steady state pharmacokinetic parameters then
you end up with a calculated dose of something like
500 micrograms of digoxin.

19

20

21

22

Q. If on the other hand the dose
were administered orally, then if I understand you
one doesn't have to posit as high a dose and it might
have been earlier in time?

23

24

25

A. That is correct. Yes, I mean
I think it should be said there is still a possibility,



D.5

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25

I mean having accused you yesterday of post hoc, ergo propter hoc fallacy, I am doing the same thing myself. I mean it is possible that something happened at 5:30, the clinical condition changed, the child was transferred to I.C.U., and at some point during the I.C.U. course a dose of digoxin is administered. However, that leaves you with a high potassium that can only be accounted for on the basis of primary disease and that is perfectly possible.

Q. Yes. Again, Doctor, that serves to indicate to me the degree of question and doubt that there has to be about this case.

Now on the assumption that we have made, for the purpose of the discussion of the last few minutes; that is to say an assumption of the administration of a dose of digoxin, that assumption could account for the elevated potassium levels I take it?

A. Yes, it could.

Q. Now, what is the effect of an elevated potassium level in the presence of an elevated digoxin level, or in response to an elevated digoxin level. Does the elevated potassium serve to dampen or reduce in some way the effect of digoxin?

A. Well, the main thing - potassium



D.6

1

2

3

4

5

6

7

(2)

8

9

10

11

12

13

14

15

16

17

18

19

20

21

22

23

24

25

is an agent that is used in the treatment of digitalis toxicity. Because one of the things that kills patients with digitalis toxicity is what this child illustrates, a block in what is called the AV node that you have probably heard of, so it is blocking conduction through that node.

Potassium tends to facilitate conduction through the node, it doesn't tend to, it does facilitate the conduction through the node. So in the presence of a high potassium conduction is encouraged. So where you see this child was in two to one block, or three to one block, that block might disappear, or might change from three to one block to two to one block, so say letting every second beat through instead of every third. This might be beneficial in maintaining circulation, maintaining cerebral function and so forth. So it is possible that a high potassium, it is probably that a high potassium here would have some protective effect.

The second aspect of that is, as I am sure you have heard again, potassium and digitalis appear to compete for binding in the myocardium. So in the presence of high potassium less digoxin is likely to be bound in the membrane system of the heart to have this toxic effect.



D.7

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25

Q Well, Doctor, in the case of Kevin Pacsai, and again assuming the administration of a dose of digoxin, do the observed elevated potassium levels and the child's structurally normal heart have any relevance in your view that the extended period from probably pre-5:30 administration until virtually 9 o'clock arrest, is acceptable, are those factors you plug into your assessment of that time frame?

A I think they have to be considered, but these factors are all so variable that you don't know how to weight them.

Q Sure.

A I mean, clearly you can look at this child as being one who was likely to be uniquely susceptible to digitalis toxicity. He had a rhythm disturbance, before anything happened he had a rhythm disturbance which was very suggestive of digitalis toxicity in Hamilton.

Q Yes.

A And he also had acidosis, which is a predisposing factor, he had had an episode of severe acidosis in Hamilton, and this is another predisposing factor to digitalis toxicity.

On the other hand I have told you



D.8

1

2

3

4

5

6

7

8

9

10

11

12

13

14

15

16

17

18

19

20

21

22

23

24

25

potassium elevation in itself has some protective effect against digitalis toxicity. The other, and the most important variable is that it just is not - the extent to which people can resist the onslaught of digitalis toxicity is just unpredictable. There are any number of cases in the medical literature of patients taking overdoses of digoxin and surviving with very high concentrations of digoxin, certainly higher than ever were measured in Kevin Pacsai, at least disregarding the Mount Sinai measurement.

So I think it is logical I think to a priori to say that this child would have been more susceptible to digitalis toxicity. But then again you have got to put that on spectrum from possible to probable. I would agree that it is probable he would have been more susceptible, but I find no difficulty with him surviving three or four hours with a concentration of maybe 15 nanograms per ml. I mean, you heard as recently as yesterday we have had children taking overdoses who survived without turning a hair with concentrations of that magnitude.

Q. With respect to the ante mortem sample that was drawn in the I.C.U., in which the level of greater than 10 was recorded; I should tell you, Dr. MacLeod, that as I understand the evidence,



D.9

1

2

in the first place Dr. Ellis' Digoxin Book shows a
computer extrapolation of the level of 10.6 nanograms.

4

But again as I understand it, it is not clear, and
that was on a 2 to 1 dilution I believe, that was

5

the assay on a 2 to 1 dilution?

6

A. Yes.

7

Q. What is not clear and I think

8

Dr. Ellis is trying to find the computer printout

9

to verify this, is whether the 10.6 was extrapolated

10

on the basis of the sample as assayed, that is to

11

say diluted, greater than 4.7, extrapolated to 10.6,

12

or whether someone had taken the computer extrapolation

13

on the diluted sample, done the multiplication and

14

said, this is the computer extrapolation as it were

15

on a neat sample.

A. Yes.

16

Q. If the former, then the

17

computer extrapolation I suppose is really about

18

21 nanograms. Now, let me ask you, against that

19

possibility and we hope we will get the answer to

20

that.

21

MR. ROLAND: I am sorry to interrupt,

22

Mr. Lamek, but this seems to be a good time to let

23

everybody know it can't be found, we have searched

24

for it and it is not available.

25



D.10

1

2

3

4

5

6

7

8

9

10

11

12

13

14

15

16

17

18

19

20

21

22

23

24

25

MS. CRONK: One of the things

Dr. Ellis suggested was he had a recollection that the police when they obtained various materials from the Hospital could have taken that as well and we are making an effort now to see whether it is elsewhere than in the possession of the Hospital.

THE COMMISSIONER: Well, we won't know the answer immediately.

MR. LAMEK: We won't know the answer immediately but I suppose we have to tackle the two possibilities.

Q. One, that the computer extrapolation was the actual level in that ante mortem sample, was a little over 10; or the possibility that it was extrapolating a level of a little over 20. Now we understand that those extrapolations are not necessarily reliable in all events. If the true level of that ante mortem sample were indeed 20-21 let us say, would that make it less likely in your view that Pacsai would have survived as long as he did, that is to say from prior to 5:30 until 8:45?

A. Yes. It would also cast quite a bit of doubt on the post mortem measurement I think.

Q. You say there is a consistency between an ante mortem of around 10 and a post mortem



D.11

1

2

of 25 which doesn't exist in the case of 20 to 25?

3

A. That is what I am suggesting.

4

5

Q. I am correct in understanding, am I not, Doctor, this multiplier effect is certainly not uniform from one person to another?

6

7

8

9

10

A. It is certainly not uniform, but it is probably universal in that virtually all the post mortem samples that are looked at show some increase in the post mortem measurement, differing orders of magnitude.

11

12

13

Q. And so on that basis I take it you would think the ante mortem level unlikely to have been of the order of 20?

14

15

16

A. Yes, I think that is unlikely.

17

18

19

20

Q. If indeed it were, and we can't discount the possibility again?

21

22

23

24

25

A. No.

Q. If indeed it were, I don't know whether you answered my question, would that reduce the likelihood that Pacsai could have survived from a pre 5:30 administration to an 8:45 arrest?

A. Yes, I think that would be less compatible with this stuttering downhill course, I would have expected a more catastrophic conclusion.

-



10nov83
E
DPra

1

2

3

4

5

6

7

8

9

10

11

12

13

14

15

16

17

18

19

20

21

22

23

24

25

Q. I suppose, on the other hand - and these things may lead us in different directions from the same assumption - again, on the assumption that the ante mortem level was in the order of 20, I take it it would make administration rather than pathophysiology the more likely explanation of the level?

A. I am not sure that that necessarily follows. Again, I think if you put it on a spectrum, you are probably right, but it is certainly not black and white. You have something going on that is sufficient to cause a very high level of potassium, a level which is, in itself, potentially lethal or definitely within the lethal range, and no one is suggesting that potassium was administered.

I am confusing you now - I am just getting even!

Q. I was thinking, Dr. Costigan raised the spectre of administration in the chart.

A. Yes.

Q. But I do not think that has been seriously suggested by anybody, you are quite right.

A. But the point I am trying to



E2

1

2

3

4

5

6

7

8

9

10

11

12

13

14

15

16

17

18

19

20

21

22

23

24

25

make - not very well - is that we are accepting a lethal concentration of potassium as occurring because of pathophysiology, a primary disease. It certainly occurred that way in Hamilton and maybe there is another cause here. I guess we have to accept, by the same token, that it is possible because of pathophysiological perturbations to have an apparently lethal concentration of digoxin as well.

Q. Yes.

A. This is, I think, what the Murphy child showed us, although that is a different situation in that it is post mortem and --

Q. I guess what I am saying here, doctor, is that, as opposed to administration versus pathophysiology accounting for the high dose, an ante mortem level of 10 still puts you on the administration as opposed to the pathophysiology explanation side.

A. Yes.

Q. With an ante mortem level of 20, I take it it will put you perhaps a little more firmly?

A. A little more firmly, yes.

Q. In other words, if we have got a level of 20 ante mortem on the one hand, it makes



E3

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25

it perhaps more likely that digoxin was there by administration rather than pathophysiological effect but less likely, on the other hand, that the child would have survived as long as he did.

Is that fair?

A. Yes, that is correct.

Q. So, the 20 level is a conondrum if, in fact, it be the right one, and it is also a conondrum with respect to the relationship with the post mortem level.

A. That is correct.

Q. The question, doctor, putting it all together, as much as we know about Kevin Pacsai and his course and the analytical findings; potassium, digoxin, all of those things, and recognizing that all of the discussion we have had recently has been on an assumption which is not necessarily valid, are you able to form any opinion as to the probable cause of death of this child - probable cause?

A. No. I think it would be very difficult to ascribe the cause in this case.

Q. If indeed - and again I ask you to make this assumption - if indeed, he did die of digoxin intoxication, are you able to form any



E4

1

2

3

4

5

6

7

8

9

10

11

12

13

14

15

16

17

18

19

20

21

22

23

24

25

opinion as to whether the digoxin was administered
accidentally or deliberately?

A. I cannot see any basis
on which one could make that judgment.

Q. When we get to Janice
Estrella, Dr. MacLeod, we become very familiar with
the problem here, knowing whether any significance
can be attached to the level of 72 nanograms recorded
in the post mortem samples from the pelvic cavity.
I do not know to what extent you are aware of the
evidence that we have heard on that issue but you may
be sure that all of the objections, proper objections,
have been raised with respect to that sample.

Do you have anything to add
with respect to it? Where do you sit with respect
to attaching any significance to the level of 72, in
light of the source of the sample?

A. I am sure I concur with
everybody you have heard before in saying it is almost
totally impossible to interpret that concentration.

Q. There is, of course, another
level recorded with Estrella, and that is a level of
greater than 4.7 in the post mortem sample drawn after
autopsy - at the same time as the other but from a
leg vein. Do you have an understanding of how that



E5

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25

sample was obtained? If you do not, perhaps I should tell you what the evidence has been.

A. I believe I know but perhaps you should tell me.

Q. As I understand the evidence, it is that the sample was drawn from the severed end of the iliac vein by the insertion of a syringe without a needle into the end of that vein, the elevation of the leg and the massaging of the leg down to the point of its being severed.

Is that your understanding of how it was obtained?

A. Yes.

Q. In light of that information as to the providence of that sample, Dr. MacLeod, what is your view as to whether any significance can be attached to the level recorded in it?

A. This is -- we don't even know a concentration on that.

Q. We know greater than 4.7.

A. Greater than 4.7 isn't the concentration, and it was not an adequate --

Q. We have got a floor.

A. We have got a floor is right. There was an inadequate sample to permit



E6

1

2

3

4

5

6

7

8

9

10

11

12

13

14

15

16

17

18

19

20

21

22

23

24

25

dilution and repetition of the test; so, I frankly think it is -- and the other piece of information we have about Estrella is that there were several measurements made putatively in the toxic concentration range prior to that. So, she had several values in life that were higher than 4.7. So, I really think that is uninterpretable.

Q. All we do know about it, doctor, is that it is a level higher than that last recorded in life. I take it that may be accounted for by some post mortem multiplier?

A. That is certainly true and, certainly, in our experience, I am sure Dr. Spielberg would have told you, we are aware of several cases in the Hospital in the last year and a half where digoxin has been stopped because of putatively toxic concentrations, and the concentration quite often continues to rise because of the child's deteriorating condition, endogenous-like substances or whatever reason.

Q. But progression here, so far as it is recorded in ante mortem samples, was a downward one, however, from the time dig. was held. Dig. came down from 9.7 to 7.8 to greater than 5 to 4.7; so there had been a downward progression.

A. Yes.



E7

1

2

3

4

5

6

7

8

9

10

11

12

13

14

15

16

17

18

19

20

21

22

23

24

25

Q. There appears to have been an elevation of some degree in the post mortem sample. For all we know, I take it that may be mere multiplier post mortem?

A. It could well fall within the normal post mortem increase.

Q. Okay.

Dr. MacLeod, I want to refer briefly to three other children, if I may, please. They are Jordan Hines, Stephanie Lombardo and Jessie Belanger. And I refer to those children because, as you know, digoxin was not prescribed for any of them so far as anybody knows.

A. Yes.

Q. Yet, digoxin was reportedly found in the exhumed tissues of each of them and in the fixed tissues of Baby Hines.

You are aware of those findings?

A. Yes, I am aware of those.

MR. LAMEK: These are all set out in Exhibit 95, Mr. Commissioner.

Q. Perhaps I can summarize them without referring to the levels because the levels may be uninterpretable anyway. But, in the case of Hines, digoxin was reported in the fixed heart tissue,



E8

1

2

3

4

5

6

7

8

9

10

11

12

13

14

15

16

17

18

19

20

21

22

23

24

25

that assay having been done by HPLC and RIA. In the case of Lombardo, digoxin was identified in exhumed tissue by HPLC and RIA and by gas chromatography and mass spectrometry and, there, the levels, for whatever they are worth, ranged from a little over 200 to a little over 650 nanograms per gram in heart tissue. In the case of Belanger, digoxin was identified in exhumed tissue, again by HPLC and RIA and GC/mass spec.

In light of those analytical results, with those analytical procedures, is it reasonable to accept that what was identified in these three children was very probably digoxin?

A. Yes, "very probably" is the right word. Ideally, as a scientist, I should say to you that I would like to see the mass spectrum but, accepting that at face value, I think there is a very high likelihood, at least in the two that were measured by GC/mass spec., that this was, in fact, digoxin.

Q. And if indeed it was digoxin, is it fair that we have to conclude that unprescribed digoxin was administered to these children?

A. Yes, a reasonable conclusion.

Q. Can one infer anything more



E9

1

2

than that from the finding of digoxin in the tissues
of these children?

3

4

A. No. I would not think that
one could go much further than that.

5

6

Q. I take it, in the first
place, it is impossible to estimate the tissue
concentration, much less any serum concentration
that may have existed at the time of death? You cannot
do that with these data, I take it?

9

10

A. No. Well, I think you
would be on very shaky ground since you simply do not
know what degree of dessication has taken place; you
don't know what the normal post mortem changes are;
you don't know the influence of bacteria. There are
many factors, as you have heard.

11

12

13

14

15

16

Q. In the case of a couple of
children, no embalming fluid either may be a factor?

17

18

A. Another confounding
factor.

19

20

Q. Dr. MacLeod, can one
even estimate how long before death digoxin was
administered?

21

22

A. No, I think not at all.
Actually, this was the point of this paper that we
got into yesterday.

23

24

25



E10

1

2

3

4

5

6

7

8

9

10

11

12

13

14

15

16

17

18

19

20

21

22

23

24

25

Q. I know. I have got my
cue right this morning.

A. This is the Ochs, O-c-h-s,
paper.

Q. The paper we marked as
an exhibit yesterday afternoon.

A. The point that I wanted to
make with this paper was that, once digoxin is
administered in a therapeutic dose or in a super-
therapeutic dose, it is bound in a variety of
tissues and simply will not disappear from those
tissues within a predictable timeframe. All the
times that you have heard in this hearing refer to
disappearance from serum or disappearance from the
plasma space, and that is a different animal than
talking about disappearance from tissues.

Q. Let us be clear on that,
Dr. MacLeod, because I confess it is a matter about
which I was totally confused. No doubt the confusion
was mine alone and everyone else understands it. But
let me be clear that I understand it.

We have heard about elimination
half life and we have been told that that can be
a period of anything from 20 to 80 hours and, in the
course of five of those half lives of whatever length



1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25

Ell 2 they may be, you will have essentially eliminated
3 whatever it is - 97 per cent or 99 per cent - of
4 the digoxin.

5 You are telling us, as I under-
6 stand it, that that refers only to elimination of
7 digoxin from the circulatory system?

8 A. That is correct.

9 Q. And does not by any means
10 indicate that digoxin which had been administered
11 and which is bound to tissue is also being eliminated
12 at that same pace, if at all?

13 A. You are correct. That
14 inference cannot be made.

15 Q. Okay. Therefore, let us
16 take a child who is on a regimen of digoxin; if the
17 last prescribed dose were a week before the time at
18 which we take a level, we may find nothing in blood
19 but that would not necessarily mean that there may not
20 be still digoxin bound to tissue.

21 Would it be pharmacologically
22 active still?

23 A. I can't say that but your
24 expectation would be that there would be digoxin
25 remaining in tissue a week after the last dose of
digoxin.



E12

1

2

3

4

5

6

7

8

9

10

11

12

13

14

15

16

17

18

19

20

21

22

23

24

25

Q. And indeed for, I take it,
a possibly very much longer period than a week?

A. I think it is impossible
to say what the actual duration would be under which
the drug remained in the tissue. Clearly, there is
some digoxin that is very tightly bound in tissues,
to receptors. There is other digoxin which is rather
loosely bound and, presumably, the loosely bound
digoxin gradually comes out and appears in the urine.
At some point, probably the tightly bound digoxin
comes out too, but that might take weeks. Again,
this is not something that has been studied, although
this paper gives us some hint of what is going on.

Shall I explain to you what this
means?

Q. By all means. It would
be helpful.

A. In the Figure 2 in the
paper, on page 509, it shows you the cumulative
amount of digoxin appearing in the urine over a period
of days, labelled across the bottom, and if you just
look at six days after the administration of the
drug, you can see that somewhere between 51 per cent
and 65 per cent of the drug has appeared in the
urine, and what this means is that the other 40 per



ANGUS, STONEHOUSE & CO. LTD.
TORONTO, ONTARIO

MacLeod
dr.ex. (Lamek)

4276

E13

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25

cent, roughly, remains in the body, and this is the
digoxin which is bound to various tissues.



F
BB/cr

1

2

3

4

5

6

7

8

9

10

11

12

13

14

15

16

17

18

19

20

21

22

23

24

25

Q. I confess, Doctor, I would infer that there is some continuing unbinding from tissue from the very fact that maintenance doses of digoxin are administered regularly to, I assume, maintain the digoxin effect?

A. Oh, yes. There must be some mechanism under which the digoxin ceases to have its pharmacologic effect.

Q. Yes.

A. But remember again we are speaking of a very small fraction of the digoxin in the body that is actually having that pharmacologic effect.

Q. Yes.

A. It may be a half of one per cent and perhaps there is other digoxin which is bound more loosely in the vicinity is a kind of a reservoir for digoxin action but if you look at this graph you can see that there is a continual gradual uphill slope on that curve between two days and six days and this represents the small fraction I think that is coming out each day from tissues. These subjects in this study were treated only once with digoxin.

Q. Well, bringing that back



1

2

then to the three children about whom we are now speaking, I take it that all that can be drawn from the analytical findings is the high probability that digoxin was administered to each of these three children at some time?

3

4

A. I think that is about as far as you can go, yes.

5

6

Q. We can say that if dig. was administered it was with respect to each of them an unprescribed dose so far as anyone can tell.

7

8

A. Yes, according to their charts, that's true.

9

10

Q. And as an unprescribed dose it may have been accidentally, it may have been deliberately administered, who knows?

11

12

A. Yes.

13

14

Q. But in the case of - well, let me ask one other question. Is the likelihood remote that an unprescribed dose of digoxin could have been administered in a non-hospital setting?

15

16

A. Yes, I would think that is remote unless there was digoxin available in the household, as there sometimes is.

17

18

Q. It is not a problem with two of the children, as I understand it, because in

19

20

21

22



3

1

2

3

4

5

6

7

8

9

10

11

12

13

14

15

16

17

18

19

20

21

22

23

24

25

the case of Baby Belanger, unless a dose was administered in the first couple of days of her life at the General, Toronto General, she spent the rest of her life at the Hospital for Sick Children and that would mean that excepting those first couple of days a dose of digoxin to Baby Belanger could have been administered at any time from November 19th, 1980 when she was admitted until December 23rd, 1980 - he was admitted, sorry - December 23rd, 1980 when he died, a period of some 35 days.

I take it, Doctor, it is your view that a dose of digoxin any time in that 35 day period could still account for the finding of digoxin in the child's exhumed tissue?

A. Oh, yes. I think given the uncertainties about the absolute concentration in those tissues, now, I wouldn't expect after 35 days to find high concentrations but there certainly would be traces and there is no question that a method like gc/mass spec. would pick those up.

Q. And in the case of Baby Lombardo who came to the Hospital for Sick Children on the date of her birth the administration could have occurred at any time between December 13, the date of her birth and her admission, until the date



1

2

of her death, December 23rd, a period of 10 days,
and I take it again an administration within that
period in your view would certainly account for
the exhumed tissue findings?

5

6

A. Would certainly give you a
qualitatively positive test for digoxin.

7

8

9

10

Q. Right. Finally, in the case
of Baby Hines, unless digoxin were administered at
North York General, again, one cannot rule out that
possibility?

11

A. No.

12

13

14

15

16

Q. If digoxin were administered
at the Hospital for Sick Children it could have been
at any time between about 11:30, I believe we
settled on the 5th of March, until the early hours
of March 8th when he died, a period of just over
two days?

17

A. Yes.

18

19

20

21

22

23

24

25

Q. Just with respect to that,
Doctor, and recognizing that the administration
could have occurred at the Hospital from which each
of these children came, we have heard a good deal
about the incidents of drug errors, as you know,
and clearly they can and do occur, no question
about it, and one has to accept the possibility that



5

1

2

3

4

5

6

7

8

9

10

11

12

13

14

15

16

17

18

19

20

21

22

23

24

25

each of these children may have received one or more doses of digoxin by error.

I have to ask you, in your view is it likely that all three of them, and I tell you with the exception of Cook they are the only three of the 36 children with whom we are concerned who were not on digoxin, in your view is it likely that all three of them received digoxin by accident or is that something about which you can form an opinion?

A. Well, I think it is entirely within the realm of possibility. I know you have had testimony from Dr. Spielberg about the occurrence of medication errors and you have had some theoretical calculations based on the number of doses of digoxin given on the cardiology ward.

Q. Yes.

A. I think it wouldn't be completely beyond the realm of possibility that three patients might have received digoxin in error.

Q. Okay. With respect, that is not quite the question I asked you. I recognize that it is possible, anything is possible?

A. Yes.

Q. Are you able to form any view as to the likelihood of this having occurred in



MacLeod, dr.ex.
(Lamek)

1

2

the case of all three of them?

6

3

A. Well, I am very loath to

4

put a number on it.

5

Q. Yes, I know.

6

A. Obviously digoxin is and

7

was one of the most commonly used medications on
that ward. Most of the patients on the ward were

8

receiving it. So, medication was being dispensed

9

frequently and if there are medication errors

10

occurring at the rates you have heard and, you know,

11

taking a conservative rate of one in every 200 drug

12

administrations being the wrong drug for the wrong

13

patient, then there is a fair likelihood that one

14

or more of these babies received digoxin in error.

15

I know, you want me to say that ---

16

Q. No, I don't want you to say

that, I want you to say what you think.

17

A. --- it is unlikely that

18

all three of them did.

19

Q. No, I don't.

20

A. Sure, it is less likely -

21

I mean, it's easier to say that perhaps one of them
did and it is easier, a little bit harder to say

22

that perhaps two of them did.

23

Q. Yes.

24

25



1

2

3

4

5

6

7

8

9

10

11

12

13

14

15

16

17

18

19

20

21

22

23

24

25

A. A little bit harder to say that all three of them did. You know, it becomes progressively less likely.

Q. Yes.

No, I don't even know whether it is something on which you have a view or could form one.

A. Oh, no, I mean, I have a view, I just told you.

Q. Say what you want to.

Okay, Dr. MacLeod, did you consider in any close way any of the other children with whom we are here concerned or has your focus been upon those we have already mentioned?

A. Well, I am not sure which other babies. I mean, I have heard about all of them at one time or another.

Q. Well, have we now dealt with the ones that you have particularly reviewed?

A. Yes, I think that is fair to say.

Q. And Dr. MacLeod, you have expressed and, if I may say so, properly expressed a number of doubts and reservations in discussing individual cases and I acknowledge obviously the



1
2 reality and the substance of the doubts and
3 reservations, let me be clear, but you have said
4 that in your best judgment, having taken into account
5 all of the reservations and questions, in your best
6 judgment Justin Cook probably received a deliberately
7 administered overdose of digoxin. That was your
8 evidence yesterday, as I understood it.

8 A. Yes, I think that is correct.

9 Q. Doctor, looking at the group
10 of children that we have talked about this morning
11 and yesterday, looking at that group as a whole and
12 in light of the view that you have expressed with
13 respect to Justin Cook, are you able to form a view
14 as to the likelihood of accidental or deliberate
15 administration of digoxin to any of the other children;
16 in other words, I guess what I am asking you is
17 this. Does your view of the Cook case serve to
18 help tip the balance of probability either way
19 with respect to any other children in your view?

19 A. Well, I can't deal with the
20 group as a whole.

20 Q. Okay.

21 A. But taking them individually
22 I think, given my judgment on the Cook case, then
23 that has to influence my judgment on the Miller case
24
25



MacLeod, dr.ex.
(Lamek)

1

2

because of the proximity in time and the circum-
stances.

3

4

Q. Yes.

5

6

7

8

9

A. And I think if we accept
that there was a deliberate overdose to Cook then
we probably have to accept a deliberate overdose to
Miller. I think really all of the other cases are
so equivocal that it would be very difficult to make
any judgment on them.

9

10

MR. LAMEK: Dr. MacLeod, thank you
very much.

11

12

13

14

THE COMMISSIONER: Thank you. Mr.
Shinehoft? Before you go, how long would you be,
Mr. Roland, if we were to call on you now?

15

16

17

MR. ROLAND: I've got a fair amount
to go through.

18

19

20

21

THE COMMISSIONER: You've got a fair
amount?

MR. ROLAND: Yes.

THE COMMISSIONER: Yes, all right.

MR. SHINEHOFT: I hope not to be
too long, Mr. Commissioner.

22

THE COMMISSIONER: Yes, okay.

23

CROSS-EXAMINATION BY MR. SHINEHOFT:

24

25

Q. Dr. MacLeod, my name is



1
2 Jack Shinehoft and I represent the parents of the
3 baby Kevin Pacsai whom you have told Mr. Lamek that
4 you reviewed his chart.

5 A. Yes, that is correct.

6 Q. I believe as well, Doctor,
7 you indicated that you were here yesterday and heard
8 Dr. Bain conclude his evidence here?

9 A. I heard the last hour and
10 15 minutes or so.

11 Q. And you were asked by Mr.
12 Lamek today about the probable cause of death of
13 Kevin Pacsai and you said you really couldn't voice
an opinion. Is that correct, Doctor?

14 A. Yes, not with any degree
15 of certainty.

16 Q. Well, could you voice an
17 opinion about the possible causes of death of Kevin
Pacsai?

18 A. Yes, I think I did that with
19 Mr. Lamek.

20 Q. Well, if you could just re-
21 iterate that, please.

22 A. Well, do you want me to
23 enumerate the possible scenarios?

24 Q. Well, no, we will get into
25



1

2

3

4

5

6

7

8

9

10

11

12

13

14

15

16

17

18

19

20

21

22

23

24

25

each of the scenarios but just initially if you could tell me in your opinion, if you have an opinion, as to the possible causes of death of Kevin Pacsai?

A. Well, I think (1) that he died of a digoxin overdose, (2) that he died of a primary metabolic disorder of some kind, (3) that he died of a conduction, cardiac conduction disturbance of unknown etiology as I read the chart, I guess, or a combination of the three.

Q. And are those the sum total in your opinion of the possible causes of this child's death?

A. In my reading. Although I really must emphasize to you that I am neither an expert in paediatric cardiology, nor even really in paediatrics since my training is in adult medicine. So, I am sure you have heard from people who are better able to judge the cause of death in Kevin Pacsai.

Q. All right. You have really concentrated on the question of digoxin overdose and the question of metabolic disorder, is that correct?

A. Or the heart disease per se, the conduction disturbance per se. I mean, we don't



1

2

absolutely know that that is derived from the other
two.

3

4

5

6

Q. I see, I see. And this
metabolic disorder is the question of the patho-
physiological problems that Dr. Spielberg has ---

12

7

A. I guess that is how it has
been referred to.

8

9

10

11

Q. And the problem that you
have with that aspect or the problem with this baby
in general is the question of potassium, is that
also correct, Doctor?

12

13

A. The potassium and I guess
the episode of severe acidosis in Hamilton.

14

15

16

17

18

Q. All right. Now, Dr. Bain
has come here and he said that this baby had some-
thing in Hamilton which caused him to have an
elevated potassium level and then something happened
in Toronto which again caused the elevated potassium
level. Would you agree with that?

19

20

A. Yes. I just don't remember
offhand how high the potassium was in Hamilton.

21

Q. Oh, I've got it and we'll
get into it.

22

23

A. We will, will we?

24

25

Q. I just wanted to know if you



1

2

agreed with that scenario as given by Dr. Bain in
his evidence?

3

4

A. Yes. I think the more
striking feature in Hamilton was the extreme
acidosis.

5

6

Q. Okay. And I understand ---

7

8

A. --- I believe went down to
6.76, very low.

9

10

Q. Yes. If I were to tell you,
Doctor, that that calculation was in error would you
agree or disagree with me or would you be able to
formulate an opinion?

11

12

13

A. In error in what sense?

14

15

Q. That the figures used, that
there was a transposition error in the calculation
of the pH level of this baby's ---

16

17

THE COMMISSIONER: He can't agree
with you on that. If you were to say something
he can perhaps change his opinion.

18

19

MR. SHINEHOFT: Yes, all right.

20

21

THE WITNESS: Yes. I mean, if it
is generally accepted that that figure is wrong I
would like to know what the right figure is.

22

23

THE COMMISSIONER: It is not generally
accepted yet; it may well be at some point. The

24

25



14

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25

way you put it to him, and you can put it to him
by all means and say if the proper - do you know
what the proper figure is?

MR. SHINEHOFT: Well, I believe there
was a transposition error. Maybe we are talking
about two different things. The pH level at one
time was 7.79, is that correct?

A. No, I don't think so.

Q. Or was it 6.7?

A. 6.79.

Q. 6.79.

A. I think I said 6.74 but it
was 6.79.

Q. My understanding is that
the figure should actually be 6.97 as opposed to
6.79 and that there was in fact a transposition
error and that very few if any children have ever
survived with the level of 6.79, is that correct?

A. That would probably be
correct. Very few survive 6.97 either, so. That
is still a very profound acidosis.

Q. Some paediatricians feel
that 6.8 is the absolute lowest level that any
child could live?

A. Yes, I couldn't argue with



15

1

2

3

4

5

6

7

8

9

10

11

12

13

14

15

16

17

18

19

20

21

22

23

24

25

that. Certainly in adults below 7 is very unusual
to survive.

Q. Yes. Okay, Doctor. Dealing
with the question of the potassium levels at
Hamilton, are you aware of his levels at Hamilton?

A. Yes, I believe the figure
is 1.8.

Q. No, no, no, I am talking
about the potassium.

A. Oh, I am sorry, potassium,
that's the question. No, I don't recall them off-
hand.

Q. All right. Well, I have
the benefit, Mr. Commissioner, of having the records
from Chedoke-McMaster and I'm not sure if the Doctor
has them or not or if Mr. Lamek has them.

THE COMMISSIONER: I take it they
are not to be found in the medical records?

MR. SHINEHOFT: I don't think so.

THE COMMISSIONER: They are not in
Exhibit 106.

MR. SHINEHOFT: I don't think they
are, Mr. Commissioner.

THE COMMISSIONER: All right. Well,
just put it in the ordinary way, say, assuming that



16

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25

the levels were ...

MR. SHINEHOFT: Well, I have them
and I can provide you with a copy.

THE COMMISSIONER: Yes, all right.

MR. SHINEHOFT: Q. It is my under-
standing, Doctor, that there were seven levels
taken at Chedoke-McMaster and the levels ---

THE COMMISSIONER: You are talking
of levels of potassium?

MR. SHINEHOFT: Seven levels of
potassium and I will give you the dates. I don't
have the times.

A. That's probably not critical.

--- --



DM.jc
G

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25

Q. Five were taken on the 8th of March; two were taken on the - one was taken the 10th and one was taken the 11th. Dealing in chronological order the levels are as follows: 5.6, 4.6, 3.1, 4.5 with slight hemolysis, 4.1, 3.9 and 5.8.

Now assuming those levels to be accurate, do you find anything alarming about those levels, Doctor?

A. The first one was 5 -- ?

Q. The first one was 5.6.

A. Yes, the two over 5 are certainly unusual.

Q. My reading, Doctor, of the textbooks on electrolytes, it would appear that the normal range is 3.5 to 5.5, any disagreement with that?

A. No, that is correct.

Q. So, would you --

A. It varies a little bit from hospital to hospital. Is that the range for Chedoke-McMaster?

Q. That is my understanding, it is the range for Chedoke-McMaster.

A. Normally, the usual potassium value is somewhere between 3-1/2 and 5. I accept



G.2

1

2

those are ranges and they go to two standard deviations

3

from the mean.

4

Q. Just those numbers alone, is

5

there anything alarming to you about those numbers?

6

A. Not especially.

7

Q. Would you say they are within

relatively normal limits?

8

A. Well, I think you can't

9

discount the 5.6 and the 5.8, those are not normal

10

potassiums.

11

Q. But there was one 4.5 that

12

was slightly hemolysized so that might have been
even lower?

13

A. Yes, sure.

14

Q. Are you aware of his potassium

15

level when he first was admitted to the Sick Children's
Hospital?

16

17

A. You can refresh my memory.

18

Q. 3.9?

19

A. 3.9.

20

Q. Is there anything alarming

about that level?

21

A. No, certainly not.

22

Q. Were you aware that in the

23

journey from McMaster, or from Hamilton to Toronto

24

25



G.3

1

2

that his IV plugged and that they had to restart it
at Toronto, are you aware of that?

3

4

A. I have heard this at some
point.

5

6

Q. That may in fact have caused
an elevation of the potassium in his body during the
trip from Hamilton to Toronto?

7

8

A. I am not quite sure --

9

10

Q. Dr. Bain says they try and
control all of this by infusing the body with IV
solution to control the potassium levels. Do you
agree with that?

11

12

13

A. Well, this is one determinate
that the potassium concentration, I wouldn't have
thought a stopped IV in transit in an ambulance
ride from Hamilton to Toronto was going to make very
much difference, but I really would have to know the
details.

14

15

16

17

18

Q. But his level at arrival is 3.9.

19

A. Yes, that is perfectly normal.

20

Q. And the hemolyzed in the 9's,
and an unhemolyzed level of 7.7, and that is in less
than 12 hours. Do you find that surprising?

21

22

A. Yes, somewhat.

23

Q. And I canvassed this with

24

25



G.4

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25

Dr. Bain, do you have any opinion as to the calculations that this child had absolutely no renal function at all, whether the body endogenously could cause that level to rise from 3.7 to 7.7, that his failure to excrete ---

A. Any absence of renal function?

Q. Yes, failure to excrete through the kidneys?

A. This is a hypothetical question?

Q. On a hypothetical.

A. Well, potassium is not in every cell in the body so I mean there can be some shifts in potassium, certainly, hemolysis, tissue necrosis of one kind or another. It would still be quite an unusual jump from 3.9 to 7.7. I think you should disregard the 9.5 whatever it is that is an artefact based on the hemolysis, but 7.7 is probably correct, a correct figure and that is a large jump, you are quite correct.

Q. Would you agree with me, Doctor, that the cause of this large jump is probably, or is one of two things, either potassium is introduced into the body or else there is a shifting of the potassium from being an intracellular fluid out to being an extracellular fluid?



G.5

1

2

A. Yes, I would agree with that.

3

Q. And that this shifting again

4

can be caused by one of two things. Either the

5

pathophysiological changes in the body, or by digoxin

6

being introduced and competing for the binding sites
at the receptors, is that correct?

7

A. Yes. I am not sure if digoxin

8

is the only potential competitor for potassium.

9

Q. The likelihood is it is one

10

of those two things?

11

A. Yes, I think in this particular

12

case that is correct.

13

Q. And you are saying in your

14

opinion you would sway 75 per cent to the likelihood

15

that it is the digoxin competing for the potassium
as opposed to this pathophysiological problem?

16

A. Yes, that is purely an intuitive

17

estimate of probability.

18

Q. Okay. Have you had an oppor-

19

tunity, Doctor, to read the Atlanta Report, the

20

unexpurgated or --

21

A. No, I haven't. Well, I have

22

read large excerpts from it, I certainly haven't read
it cover to cover.

23

Q. Did you read that part of the

24

25



G.6

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25

report that is in relation to Kevin Pacsai?

A. I probably read it a few months ago, but if you want to ask me something specific --

Q. I wondered if you recall reading anything about pathophysiology problems, or was it ever raised in the Atlanta Report that you are aware of?

A. I can't honestly remember.

Q. Do you know if it was raised by Dr. Kauffman as applicable to Kevin Pacsai?

A. No, I don't believe he mentioned it.

Q. And Dr. Hastreiter?

A. I haven't specifically seen Dr. Hastreiter's comments on Pacsai.

Q. Did Dr. Hastreiter testify at the Preliminary Hearing of Susan Nelles?

A. Yes, he did.

Q. Were you aware of the evidence that he gave at that Preliminary Hearing?

A. I had it, I am sure I read it a year and a half ago but I really don't remember.

Q. Both of these doctors are clinical pharmacologists?

A. No, Dr. Kauffman is a clinical



G.7

1

2

pharmacologist, Dr. Hastreiter is a cardiologist.

3

4

5

MR. ROLAND: Mr. Commissioner, we are going to have these witnesses come and talk to us and we can have their views about it directly and we all can ask them.

6

7

8

MR. SHINEHOFT: I am aware of that. I am just wondering if Dr. MacLeod has read their views and what they have to say.

9

10

11

12

13

Q. Are you aware, Doctor, of any other clinical pharmacologist that has raised this possibility as far as the death of Kevin Pacsai; that is the question of this pathophysiological problem, other than Dr. Spielberg?

14

15

16

A. Well, no, but I am certainly not privy, I have no idea how many clinical pharmacologists may have looked at the data. I am not sure how I can possibly answer your question.

17

18

19

20

Q. Is this theory more prevalent with a child who may have a renal dysfunction, or renal problem, than a child who has a normal renal function?

21

22

23

24

25

A. Well, I will be honest with you, I don't think that any of us feel we are even talking about a specific disease entity, so it is very difficult to answer your question. We are not talking



G.8

1

2

about some well defined pathophysiological abnormality.

3

It may be that Kevin Pacsai, for instance, had in

4

some way unusual binding proteins with an affinity for

5

digoxin. Perhaps had less affinity for proteins

6

than in other patients. Perhaps he was more

7

susceptible to the effects of potassium on that

8

binding. I don't know, it is a very nebulous

9

concept, I quite agree with you.

10

Q. Yes.

11

A. Whether or not renal function

12

would change that I don't know. I think there is

13

some suggestion in Kevin Pacsai's chart and in

14

Dr. Kauffman's report that he probably had some

15

abnormality of renal function in that his creatinine
is 1.3, isn't it, at the time of death?

16

Q. Yes.

17

A. And that is a little high.

18

Q. But his BUN is normal?

19

A. That is not a very reliable
indicator, the creatinine is certainly much better.

20

Don't misunderstand me, I am not suggesting he is
in renal failure at that time.

21

Q. So you are saying that this

22

theory is somewhat nebulous and has not been crystal-

23

lized and not much in the literature has been reported

24

25



G.9

1

2

on this until recently, is that a fair statement?

3

4

5

6

7

8

9

10

11

12

13

14

15

16

17

18

19

20

21

22

23

24

25

A. I am sure even now nothing has been reported. I am not aware of any case description in the literature which could be said to be exactly analagous to Kevin Pacsai. It may be that he is completely unique.

Q. Just the same as Gary Murphy was completely unique?

A. Gary Murphy was unique as well.

Q. But there is one thing that we know, and that he had an ante mortem level of greater than 10 as far as digoxin was concerned?

A. Yes, that is correct.

Q. And we know that the therapeutic level of digoxin is 1.5 to 2.5?

A. I think for children you put the range a little wider than that, but most people would accept 3, or even 3.5 as being within a therapeutic range for some children.

Q. So assuming even a level of 3, the level of 10 is three times greater than the normal therapeutic level, is that correct, Doctor?

A. Yes, that is correct.

Q. It may very well mean that this child did die of digitalis toxicity, you are not



G.10

1

2

in a position with the knowledge and state of the
art that you have to say definitively "yes" or "no",
is that correct?

4

5

A. That is correct.

6

7

MR. SHINEHOFT: Thank you very much,
Doctor.

8

9

10

11

12

13

14

15

16

17

18

19

20

21

22

23

24

25

THE COMMISSIONER: Thank you,
Mr. Shinehoft. For the benefit of anybody who wasn't
here at the beginning, we are going to take our break
now for 20 minutes, but because of all our scheduling
problems we have cancelled the argument for this
afternoon and we hope to reschedule it for Tuesday
after I give judgment in the two matters upon which
there is written argument, and we will continue with
Dr. MacLeod today in the hope that we will complete
him because he is not available all of next week.
We will not be sitting anywhere on Monday, we will
be sitting here on Tuesday and we will not be sitting
anywhere on Wednesday, Thursday and Friday of next
week. Now I know that is a sudden change but that
has all been dictated by things we didn't know about
yesterday. I will certainly hear any representations
if anybody wants, after you have had time to digest
it, but we will take 20 minutes.

--- Short recess



H/DP/ko

1

2

THE COMMISSIONER: Yes, Mr. Olah?

3

4

5

6

7

8

9

10

11

12

13

14

15

16

17

18

19

20

21

22

23

24

25

MR. OLAH: I have a concern, I am

sorry I was late this morning but I had a chance to
review your comments by the magic of videotape,

Mr. Commissioner. I am somewhat concerned about the
change in plans, for obvious reasons. Number one, I
certainly had not prepared to cross-examine Dr.

MacLeod because I thought we were arguing this
afternoon, but that is not a major concern to me.

The more major concern to me is that
we have been trying to arrange this argument for some
three weeks to get Mr. Sopinka and Mr. Percival
available. Now, I am told by Mr. Brown that he is
going to have some information with respect to
Mr. Sopinka and his availability but if he is not
available Tuesday, Mr. Commissioner, I would be very
concerned, because I have been trying to get an
argument before you, sir, and some sort of a ruling.

THE COMMISSIONER: It is not that
wildly urgent, though, the question of the notice, is
it?

MR. OLAH: I am sorry, sir?

THE COMMISSIONER: The question of the
notice is the matter that you are most concerned with?

MR. OLAH: That is correct.



1
2 THE COMMISSIONER: That is not that
3 urgent, is it?

4 MR. OLAH: Mr. Commissioner, to my
5 client it is, even though you may reach certain
6 conclusions on the issue of naming names, as you
7 have called it, it does have concern because it has
8 radically altered her position and rôle in this
Commission.

9 THE COMMISSIONER: I am sorry, in my
10 view it has not changed one iota.

11 MR. OLAH: I know that you and I
12 disagree on that point, sir, but I had hoped to
13 persuade you otherwise. It is a matter of concern
14 and so --

15 THE COMMISSIONER: Well, we are going
16 to try and do it Tuesday morning, I have suggested
17 that, but remember I would not think that Mr. Sopinka
18 is as interested as you are in the notice question
19 and if you can go on Tuesday morning the only thing
20 he is interested in is the police report, and you are
21 not as interested - I do not imagine you are
22 interested in the police report at all, except out
23 of idle curiosity.

24 MR. OLAH: Idle curiosity has had a
25 prominence in this matter.



H 3

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25

THE COMMISSIONER: I would think that that is not a problem. If we can go on on Tuesday morning with the argument, I don't think we need to have Mr. Sopinka there for that.

MR. OLAH: I thought that Mr. Sopinka was going to take a position on the notice issue also, but I may be in error. Maybe Mr. Brown could help us on that.

THE COMMISSIONER: I don't think he can - if there ever was a case where he has been notified of the problem, this I think would somewhat head the list. To say that he has no idea why he is here would strain credibility a little.

MR. OLAH: It is not a question of no idea why you are here, Mr. Commissioner, it is a question of compliance with Section 5(2) which is quite different, in my respectful submission.

THE COMMISSIONER: I know. There is a mild judicial problem but it is not a prejudicial problem. That is all I am trying to say is that I don't really believe anybody is prejudiced if we don't go on with it right away and I will go on with it on Tuesday if we can, and it may not matter whether Mr. Sopinka is available or not - if you are available.



11 4

1

2

3

4

5

6

7

8

9

10

11

12

13

14

15

16

17

18

19

20

21

22

23

24

25

MR. OLAH: I am available and as long as we are prepared to proceed Tuesday I am pleased but I would not want to have a reoccurrence of a delay where we are into December or January before we can get this matter before you.

THE COMMISSIONER: No, all right then, I will bear that in mind. Yes, Mr. Brown?

MR. BROWN: I have spoken to Mr. Young and apparently Mr. Percival may be available on Tuesday. I will know by early this afternoon whether Mr. Sopinka is.

In the event that he is not, may I again suggest that after the meeting this afternoon that argument on the police report be heard. It is difficult to get the two of them together to schedule the matter.

THE COMMISSIONER: You mean we hear the argument this afternoon?

MR. BROWN: Yes.

THE COMMISSIONER: It depends upon whether we can finish Dr. MacLeod.

MR. BROWN: If it appears that Dr. MacLeod may not finish today, I submit that perhaps he could be rescheduled to some later date.

THE COMMISSIONER: We will work on



1

2

3

4

5

6

7

8

9

10

11

12

13

14

15

16

17

18

19

20

21

22

23

24

25

H 5

that, but you have heard the problems of scheduling
and it is going to very, very difficult to fit him in.

MR. BROWN: I appreciate that but
there is precedent for splitting a witness' evidence.

THE COMMISSIONER: Oh, yes, this
Commission has given precedence for just about any-
thing.

Mr. Roland?

EXAMINATION BY MR. ROLAND:

Q. Mr. Commissioner, first of all
I have distributed two more papers that I will have
the witness identify. One is a response to a request
from Commission Counsel and was provided to them and
it is a Study of Unit Dose Drug Distribution in Four
Canadian Hospitals. Dr. MacLeod produced this study
at the request of Commission Counsel.

A. Yes.

MR. ROLAND: Could that be marked as
the next exhibit please?

THE COMMISSIONER: Yes, Exhibit 255.

--- EXHIBIT NO. 255: Study of Unit Dose Drug
Distribution in Four
Canadian Hospitals, produced
by Dr. MacLeod.

MR. ROLAND: Q. And the second paper
is Progesterone Derivatives that Bind to the Digitalis
Receptor and it is a paper that is published by



H 6

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25

The American Society for Pharmacology in Molecular Pharmacology. Is that a paper that you produced, Doctor?

A. Yes, it is.

MR. ROLAND: Could we mark that as the next exhibit, please?

THE COMMISSIONER: Exhibit 256.

--- EXHIBIT NO. 256: Paper entitled: Progesterone Derivatives that Bind to the Digitalis Receptor, published by The American Society for Pharmacology in Molecular Pharmacology.

MR. ROLAND: Q. Doctor, dealing with Exhibit 255, the study of unit dose drug distribution in four Canadian hospitals, for our purposes would you turn to page 88 and briefly indicate to us from the study what is concluded with respect to medication errors?

A. Yes. The important information I think is all on Table 5 and probably it is the line in the middle of that table that concerns you, that the error rate, excluding wrong time errors, and this is a comparison between four Canadian hospitals, phase one being before the introduction of a unit dose system and phase two being after the introduction of such a system. I think you can see, looking across that line, that the error rates are high in both



H 7

1

2

phases, a little bit lower in three out of the four hospitals, after the introduction of unit dose.

3

4

Probably the important point is in a non-unit dose hospital the error rate ranges between 8.9 percent and 14.5 percent.

5

6

Q. Yes?

7

8

A. These hospitals, the actual nature of the hospitals is listed in the Introduction.

9

10

11

12

13

Q. Yes, I see that hospital A is an 85 bed general hospital in Saskatchewan; hospital B is a 183 bed general hospital in Newfoundland. I am not sure about hospital C because it seems to be Xeroxed off the top of page 86 but I presume it is something in the neighbourhood of 300 or 400 beds.

14

15

A. It is a non-teaching hospital in an urban centre in Manitoba.

16

17

18

Q. And then hospital D is a 592 bed general hospital in, presumably Toronto, or another urban centre in Ontario?

19

20

21

22

23

24

25

A. Yes.

Q. And from the study, as I read it, we are not able to tell the kind of errors that are included in the error rate excluding wrong time, but it is presumably all kinds of errors, apart from wrong time?



H 8

1

2

A. Yes, it is a catchall.

3

4

5

Q. And then there is no breakdown with respect to those errors in the study itself and presumably it ranges from very modest kinds of errors to rather serious drug errors?

6

7

A. Yes, I think that is correct.

8

9

Q. With respect to the next exhibit, 256, can you tell us, Doctor, what this study discloses?

10

11

12

13

14

15

16

17

18

19

20

21

22

23

24

25

A. I think the only point that really needs to be made is that there are probably hundreds of such



1

2

3

4

5

6

7

8

9

10

11

12

13

14

15

16

17

18

19

20

21

22

23

24

25

compounds existing in nature that are potential candidates to be the endogenous dig.-like substance - just in case anybody had the idea that there was maybe one specific thing that we are looking for.

Q. Is the structure of digoxin shown on that page?

A. No, it is not on that page at all but that is the basic steroid nucleus that is central to digitalis.

Q. Turning to the evidence that you have given so far, and some of the other evidence that we have heard, with respect to Kevin Pacsai we have heard that adrenal insufficiency may have some effect on potassium, and raise the potassium level. Does digoxin itself have any effect on the adrenal glands?

A. It has. It has been shown very recently in fact to affect the adrenal hormones that in turn regulate potassium. It is probably not correct to say that it has a direct effect on the adrenal gland but it certainly decreases a hormone called aldosterone and when that happens potassium goes up. It has been shown to do this acutely following an intravenous dose in normal volunteers.

Q. And with respect to Kevin Pacsai,



H 10 1
2 you have told us that his decline, beginning on the
3 ward and then when he was transferred down to the
4 ICU, was one that was not sudden and dramatic but a
5 rather progressive decline over a number of hours.

6 Do I understand your evidence that in
7 your view if we were talking about digoxin toxicity
8 or the effects of digoxin that that is consistent more
9 with an elixir administration rather than IV
administration?

10 A. In my view it is, yes.

11 Q. I take it then from an IV
12 administration you would have a more sudden and
13 dramatic effect from the digoxin?

14 A. Yes, I think I should qualify
15 my answer. When you say an IV dose I assume you are
16 talking about a rather large IV dose, several times
17 the therapeutic. Of course, there would be no way to
18 distinguish between an intravenous administration of
19 a relatively small dose, therapeutic dose, versus the
administration of an oral dose.

20 Q. With respect to Kevin Pacsai,
21 Mr. Lamek has taken you through the various
22 possibilities, given the numbers, that is a greater
23 than 10 ante mortem reading obtained in the ICU at the
24 time he was first transferred there and then the post
25



H 11

1

2

3

4

5

6

7

8

9

10

11

12

13

14

15

16

17

18

19

20

21

22

23

24

25

mortem level of 26, and he has indicated to us that the evidence raises the possibility that that ante mortem level of greater than 10 may indeed be something in the neighbourhood of 20.

You have told us that that would, in your view, be less likely, given the post mortem reading of 26, and the fact that there was this rather slow decline or regular decline as opposed to a dramatic event.

- - - -



BmB.jc
I

1

2

3

4

5

6

7

8

9

10

11

12

13

14

15

16

17

18

19

20

21

22

23

24

25

Q. But I gather that ante mortem reading of greater than 10 may be at steady state and it may be at some stage on the alpha curve?

A. Yes. It becomes much harder to interpret. If it is at some point on the alpha phase it might in fact represent an alpha phase concentration following really a relatively small dose of digoxin.

Q. Yes. And the possibility was raised that there was another dose of digoxin given in the I.C.U. either by intravenous or I presume it could have been given as well if it was by elixir. Can you tell us, is that possibly consistent with the post mortem reading of 26?

A. It certainly could be.

Q. Yes.

A. I mean, there could be two doses administered. There could be any number of doses I suppose. There could be a sequence of small doses and you could still have these values. What we are confronted with again is the difficulty of interpreting an isolated concentration measurement and trying to make all sorts of inferences about what went on in the hours before or after those concentration measurements and I think you could draw any



I.2

1

2

number of graphs that would explain these two
concentration measurements quite satisfactorily but
you would have to make a lot of assumptions.

3

4

5

Q. As I understood your evidence
the Gary Murphy case somewhat has altered your
perception of the Kevin Pacsai case, is that correct?

6

7

8

9

10

11

12

13

14

A. Yes. You know, I say that I
guess primarily on an emotional basis that we were
confronted with concentration measurements that are
of the same order of magnitude as those seen in Kevin
Pacsai and we were prepared to believe that those
concentrations had come about primarily on a patho-
physiologic basis. So, this tends to change your
thinking about Pacsai.

15

16

17

18

19

20

21

22

23

24

25

Q. Let's turn to post mortem
multiplier. We have heard in evidence that it is
generally accepted that there is a post mortem
multiplier effect for serum levels in measuring
digoxin of about 2 to 4, something in that neighbourhood,
as compared to ante mortem levels. Most of the
literature and I think most of the discussion in
evidence has dealt with therapeutic ranges of digoxin
in ante mortem serum in the range of 1 to 3 or so and
then we have seen a multiplier effect, in fact, in
Exhibit 232, which is the study done at the Hospital



I.3

1

2

3

4

for Sick Children, we have seen the post mortem readings that show I think on average a multiplier effect of something in the neighbourhood of 3.8?

5

6

7

8

9

10

11

A. Yes, our figure is 3.8, the mean multiplier effect on that data, but you would have to be a little bit - you have to pick and choose which ones you include and which ones you don't. You understand that one of the difficulties with deriving any kind of multiplier is that the pre mortem values are usually not taken in very close proximity to death. So, we don't know precisely what figure.

12

13

14

15

16

17

Q. We are also confronted here with some very high post mortem levels 72's and 78's and the Inwood case, 491, and presuming those are all, there is no artefact involved and so on, those are accurate post mortem levels. Does the same multiplier factor in your view work in trying to arrive at an ante mortem figure?

18

19

20

21

22

23

24

25

A. I have no way of knowing that. Intuitively, and my intuition is no better than anybody else's, I would think that it would be unwise to apply the same multiplier when you get up into that very, very high range as you would apply to more therapeutic concentrations. So, in other words, I'm not sure if you've got 75 you can say, well, that



I.4

1

2

3

4

5

6

7

8

9

10

11

12

13

14

15

16

17

18

19

20

21

22

23

24

25

is probably four times higher than it was pre mortem. It probably is higher but I imagine it is, you know, 25 per cent higher or 50 per cent higher but it is not likely to be four times as high as the pre mortem value. But I must emphasize that is pure intuition I am talking about. I am unaware of any study that looks at that.

Q. You would intuitively then use a much smaller multiplier factor than 2 to 4?

A. I would, yes.

Q. In those ranges?

A. Yes.

Q. I see. All right, turning to another subject, it has to do with the alpha curve and, in particular, the alpha curve of showing the digoxin distribution in Exhibit 254, which is a paper you have introduced. Let me ask you about the infusion time that is involved in administering digoxin when it is injected into the buretrol. I gather that when it is injected into the buretrol and administered in that manner that it would take some time to infuse into the infant and that time may range in the neighbourhood of an hour or perhaps more or less?

A. Yes, it can range over any time.



I.5

1

2

3

4

5

6

7

8

9

10

11

12

13

14

15

16

17

18

19

20

21

22

23

24

25

All the buretrol really is is a smaller volume reservoir that has been put into the line. I mean, you can empty that reservoir as quickly or as slowly as you wish but the usual thing in administering intravenous solutions to younger children is to run it quite slowly.

Q And in Exhibit 254 I see that the infusion time there was by pump over a period of one hour.

A Yes.

Q Am I correct in assuming that the longer the infusion time the lower the point is on the alpha curve that you begin the curve?

A Yes. No, if you make the infusion time slow enough then you really just mimic the absorption after oral administration. So, at some point the intravenous curve becomes exactly the same as the oral curve. If you are pumping it very, very slowly, say, 1 ml of solution per hour into a vein it is going to be no different from the absorption.

Q I gather though the net effect of that is that the slower you infuse the digoxin by means of the IV the lower the highest point is on the graph?



I.6

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25

A. Yes. Yes, I think this is illustrated in those curves. If you look actually with a half a milligram, the peak that they measured is 10 nanograms per ml, with 1 milligram it is about 20 and with 1-1/2 milligrams it is 30. So, they are in proportion but if they had taken a measurement half an hour before that at the time when the pump was actually running and they were infusing it, the levels would have been somewhat higher or back further up the alpha curve.

Q. Yes.

A. You can't be precise because again, because of this mode of administration you are flattening that peak out a little bit. You don't get peaks as high as you would see after a relatively rapid intravenous administration, say, over five minutes or ten minutes.

Q. And is it also correct that the slower the infusion the longer it takes to reach the maximum effect of the digoxin?

A. Oh, yes, certainly this would be delayed. You know, the comments that are made about time to peak effect after intravenous administration all presuppose administration over about five minutes.



I.7

1

2

3

4

5

6

7

8

9

10

11

12

13

14

15

16

17

18

19

20

21

22

23

24

25

Q. And administration over five minutes is not likely to be administration by injecting the digoxin into a buretrol?

A. No, not at all. It really would not normally be used that way. The intravenous use of digoxin is relatively limited anyway. When it is used it is used for the treatment of cardiac rhythm disturbances and usually there is an element of emergency there. So, you want to see the effect promptly, so, you give it over five minutes and you would expect to see the effect in 15 minutes. That is really the only use of intravenous digoxin that is clinically accepted.

Q. I take it then if it was to be administered as you say over a period of five minutes that would be done by injecting it into the IV line, would it?

A. That is correct, directly into the line.

Q. Yes. And would there be some pump that regulated the infusion of it into the child?

A. In some cases, there might be. Nowadays it is quite common, there are miniature pumps that are readily available and often we pump drugs in but the pumps are expensive and not available,



I.8

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25

so, sometimes it is put in by hand. The timing of the infusion is not critical usually.

Q Well, we have heard evidence from Dr. Spielberg that there is a real risk of injecting it too rapidly in the IV line and then pushing it into the child by what is called an IV push?

A Yes.

Q The danger there is the effect we were told of propylene glycol and you have agreed with that evidence?

A Yes, I think that is correct.

Q And is it the therapeutic procedure to push it into the child or to simply inject it into the IV line and let it infuse in?

A Well, it depends. It depends to a degree on how fast that intravenous infusion is running under normal circumstances. So, you are coming to give a drug into a line you've got an infusion going through that line at some rate, it wouldn't make much sense to put it slowly into the line so that the drug is all sitting in the line and then open the valves and then let it pour in at a great rate. So, how you handle that infusion depends a little bit where the injection site is. So,



I.9

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25

usually on the line there is more than one injection site; there is one that is fairly high up the line, there is one that is a little closer to the baby. If you are giving it in the one that is close to the baby you are in essence giving the drug directly into the baby's circulation and there you would clamp off the line above, give the drug over five minutes perhaps with the idea that it was going straight into the baby, then you open up the line and let it run again at the rate you were using before.

Q. Right.

A. But that is the simplest situation. If you are putting it in higher up the line then you have got to be very careful that you don't inadvertently give a rapid push just by opening it up too fast.

Q. All right. Let's turn to some pharmacokinetics of digoxin. You have told us about specific and non-specific binding of digoxin. As I understand your evidence, the specific binding occurs when you are referring to specific binding, you are referring to the binding at the ATPase sites of the cells and that is primarily the heart?

A. Yes. Well, that is what is



I.10

1

2

accepted as the receptor for digoxin.

3

Q. Yes.

4

5

6

7

8

9

10

11

12

13

14

15

16

A. So, that in a sense, it is certainly specific in the sense that it is that binding that leads to the pharmacologic action of the drug. There may in fact be a number of other proteins in the body, and there may be different proteins in different tissues that will also bind to digoxin in a very specific fashion, that is, with quite high affinity. There may also be a lot more proteins of various kinds that bind in a very non-specific fashion and fairly loosely to digoxin and there is some distribution amongst these various binding sites for digoxin. But most people when they refer to the specific binding are thinking primarily of the digoxin receptor, the sodium potassium ATPase.

17

18

Q. Yes. And you have told us that that is the therapeutic effect that you are looking for?

19

20

21

22

23

24

25

A. That is the receptor, that is the binding which is going to translate into pharmacologic action or toxic action of the drug.



10nov83
J
DMra

1

2

3

4

5

6

7

8

9

10

11

12

13

14

15

16

17

18

19

20

21

22

23

24

25

Q. And with respect to
non-specific binding, I take it that has no
therapeutic effect?

A. As far as we know. I mean,
it is of low affinity and probably not associated
with any pharmacologic action, and that is partly
why we call it non-specific.

Q. And that is what we are
referring to when we talk about digoxin distributed
in the skeletal muscles and so on; all of that is
non-specific binding, I take it?

A. It is certainly not known
to have any pharmacologic action at that site, so
it is probably non-specific, although the affinity
of the binding may still be quite high.

Q. That digoxin, I take it,
that is found bound to the proteins, protein molecules?

A. The digoxin presumably
binds to proteins in the membranes on the outside of
the muscle cells.

Q. Yes.
Is this same non-specific binding
in the heart?

A. Oh, yes, certainly.

Q. Can you tell us --



J2

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25

A. There may be more, relatively more specific binding in the heart than in some other tissue in that there is more sodium potassium ATPase there.

Q. Yes.

A. But sodium potassium ATPase is found in every tissue in every membrane in the body so it is not something that is peculiar to the heart.

Q. So, there is both specific and non-specific binding then throughout the body?

A. In every tissue.

Q. What is the percentage, roughly, of specific binding compared to non-specific binding?

A. It is difficult to say it with any certainty, but probably somewhere between 1 per cent and 3 per cent of all the binding is specific, but the great majority, the major part of the binding is non-specific. It may be as little as half of 1 per cent. I may have used that figure yesterday. It is pretty hard to quantify.

Q. You told us that the bond itself, I gather, is stronger with specific binding?

A. One would assume this, and, again, it is an assumption, but that is a high



J3

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25

affinity binding. There may, as I guess I suggested a few minutes ago, be other high affinity binding sites that don't lead to any pharmacologic action; so, affinity, per se, doesn't necessarily make it specific, at least not specific in the sense of leading to pharmacologic action.

I hope I have got you suitably confused!

THE COMMISSIONER: There is no action on anything but the heart, I take it?

THE WITNESS: No, that is not correct. There are actions, in fact, in many, many tissues. Certainly, probably most of the tissues in which it is found. There is no question there are actions in the central nervous system and the brain - they are not beneficial actions but they are toxic effects. There certainly are actions in the red blood cells, where we know --

THE COMMISSIONER: You are talking about digoxin now?

THE WITNESS: I am talking about digoxin. Certainly, there are actions in the kidneys. This is what causes the potassium to go up.

THE COMMISSIONER: I see.

THE WITNESS: And primarily, there



J4

1

2

3

4

5

6

7

8

9

10

11

12

13

14

15

16

17

18

19

20

21

22

23

24

25

is an action, as we discussed a few minutes ago, to change the level of aldosterone, an adrenal hormone. There are a lot of pharmacologic actions of digoxin that have nothing to do with the heart.

THE COMMISSIONER: Are they serious?

THE WITNESS: Well, they may account for much of the toxicity that is described, particularly now talking about the chronic type of toxicity, the toxic reactions you see in patients who have been taking digoxin by mouth for years and gradually developing some side effects. The beneficial effect is entirely in the heart.

THE COMMISSIONER: But I take that even if - and I don't imagine this can happen; there would never be a case of the digoxin binding to other parts and not binding to the heart?

THE WITNESS: I can't imagine that happening, no, not at all.

MR. ROLAND: Q. So, when you talk about the effect, whether it is therapeutic or toxic, beneficial or not beneficial, in various tissues of the body, you are talking about the specific -- it is thought you are talking about the specific binding of digoxin; that is, to the ATPase?

A. Yes . I have been using



J5

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25

specific in the sense of binding to the ATPase and producing a pharmacologic effect. That may not be -- you get ten pharmacologists here and you will get ten different interpretations. It is probably safer to talk about high affinity binding and low affinity binding. High affinity binding perhaps represents 3 per cent to 5 per cent of all the digoxin bound in the body. Low affinity binding represents everything else - digoxin that is found in skeletal muscle, liver, kidneys.

Q. So that when we are talking about movement of digoxin from tissue back into serum, I take it, because of the percentages you have already told us about and because of the affinity, the relative strength of the bond for specific as compared to non-specific binding, the movement, both in percentage and because of the relative strength of the bond, is largely from or much greater than non-specific than specifically bound digoxin?

A. Yes. I think that is correct, certainly from low affinity. The digoxin which is removed early, if you look at that graph, in that reference I mean, you can see that in the first day 30 per cent of the digoxin dose disappears. That is clearly digoxin that was bound with relatively low



J6

1
2 affinity in various tissues and has been available
3 to come back into circulation and be cleared by the
4 kidneys. The digoxin which remains behind, the
5 digoxin which is coming out six days later, that is
6 digoxin that was bound with high affinity in heart,
muscle or some other tissue.

7 Q. So, when we are talking
8 about -- when you are telling us in relation to
9 Babies Lombardo, Belanger and Hines about not being
10 able to determine when the dose, or doses, of
11 digoxin were given to those three babies, because we
12 only have readings from the exhumed tissue, what you
13 are really referring to, I gather, is the fact that
14 digoxin bound to ATPase and specifically bound to,
15 perhaps, some proteins may remain in tissue, they are
bound for a great long time?

16 A. Yes, I think so.

17 Q. And it is because of the
18 nature of the binding, I gather?

19 A. Yes. It is a very high
20 affinity bond, and I can't tell you the absolute
21 duration of that, but it is certainly longer than six
days.

22 Q. And when we are talking
23 about agonal events - and let's for instance refer
24
25



J7

1

2

3

4

5

6

7

8

9

10

11

12

13

14

15

16

17

18

19

20

21

22

23

24

25

to the Miller baby, where there seemed to be some damage done to Baby Miller's heart in the resuscitation process - and the likelihood or the possibility that some digoxin was redistributed from tissue to serum, I gather what we are talking about is that 97 per cent more likely -- we are talking about that 97 per cent of digoxin that is not specifically bound?

A. Yes. I think that is correct. It is the low affinity bonded digoxin that is likely to be released in those circumstances, unless you get to the situation where you have absolute destruction of tissue, where tissue becomes mascerated; the tissue dies, in which case, you know, no bond is going to survive that.

Q. You indicated in your evidence at the preliminary hearing and again in questioning from Mr. Lamek that there may also be some redistribution post mortem from serum to tissue.

I take it that is not a binding phenomenon; that is simply that the digoxin may migrate into the tissue from the serum in some fashion in an unbound way?

A. Well, it will only migrate into tissue; you would never be able to detect this unless it was held there. It would



J8

1

2

3

4

5

6

7

8

9

10

11

12

13

14

15

16

17

18

19

20

21

22

23

24

25

certainly be low affinity type binding or non-specific binding. I think if you mix up digoxin with membranes, you are going to find that some of it sticks to the membranes, and that is really all I am talking about.

Q. I gather from your evidence that you think that is a very minimal phenomenon; that is not going to occur to a great degree at all?

A. I certainly think it would be minimal with any kind of normal concentration of digoxin. If we start talking of concentrations of 491 nanograms per ml. sitting in the ventricular cavity, then I think it becomes a possibility.

Q. Let's turn to Baby Cook.

Mr. Lamek, in great detail, took you through the timing of the events that occurred around the period of arrest and death for Baby Cook. You indicated, as I understand it, in your evidence that the most likely timing for a dosage of digoxin of 1 or less than 1 adult ampoule was between 3:45 a.m. and 4:26 a.m.

A. I think that is correct.

Q. And you arrived at that conclusion I gather, from looking at the serum numbers and the fresh tissue levels for digoxin?



J9

1

2

A. Yes, that is correct.

3

Q. And you told us that in

4

your view, it is unlikely that the propranolol

5

dosage which was given at 3:45 was digoxin in error.

6

I understand from your evidence

7

that you arrived at that conclusion because there are

8

too many errors that would have to be made to have

confused digoxin for propranolol?

9

A. I think I was referring,

10

to be absolutely correct, to the possibility of error

11

in drawing up propranolol into that syringe which was

12

taped to the bed.

13

Q. Yes.

14

A. I find that an unlikely

error to have occurred.

15

Q. Let me ask you, if digoxin

16

was intentionally drawn up in that syringe and taped

17

to the bed, would you view that syringe containing

18

digoxin as a likely mode for intentionally killing --

19

I shouldn't say intentionally killing; I should say

20

intentionally administering a dose of digoxin to

Baby Cook?

21

A. I think that would provide

22

an ideal opportunity to administer it, yes.

23

Q. And I take it you say that

24

25



J10

1

2

3

4

5

6

7

8

9

10

11

12

13

14

15

16

17

18

19

20

21

22

23

24

25

because the timing is within, it is right at the minimum time that you place for administering -- I'm sorry, the maximum time.

A. Yes, the maximum time. The timing would be appropriate. I think you would have to--in order to make that hold water, you would have to assume that the alpha phase is a little bit prolonged, and that is not hard to assume because this baby really had a failing circulation and was in cardiac arrest for part of that time. So, it is quite possible that the alpha half life is a little bit longer than the kinds of time you have been told. It might be easily 45 minutes, say, instead of 20 minutes, or 25 minutes. So, it is quite possible to have administration at that time.

Q. And we know that there were two dosages of what was purported to be propranolol; one of .2 ml. and one of .4 ml., given, I think, at 3:45 and then again at 4:45.

If we take those combined doses -- I'm sorry, 3:45 and 3:55.

A. Yes.

Q. That is ten minutes apart.

A. Yes.

Q. Mr. Lamek corrects me by



J11

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25

reaching for his book.

If you take those combined dosages of .6 ml., is that a sufficient volume if translated into digoxin, is that a sufficient volume or amount of digoxin to produce the numbers for serum digoxin and the fresh tissue levels in this case?

A. I think it probably would fit. I would have to do some calculations, but I think -- Again, if you make some assumptions about slowing of the distribution phase, I think it is possible.

Q. I think this is in evidence, but we are correct, I gather, in assuming that, once that propranolol or digoxin is in the syringe, they are indistinguishable by looking at them?

A. Yes, I think that is correct.

Q. Let's turn to the phenomenon of seizures in a number of these babies.

We have heard from Dr. Bain that in something like sixteen or seventeen of the babies, there is found in the charts notations of seizures. We found those notations, particularly with respect to



J12

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25

Babies Miller, Cook, Estrella and Pacsai, there is some question about that. There is a question mark where it says "seizure" on the Pacsai chart, but there seems at least to be a notation of seizures.

Can you tell us, from your own experience and your knowledge of digoxin toxicity and your review of the literature, are seizures consistent with digoxin toxicity?

A. I am not aware that anybody has ever reported seizure activity as being a specific feature of digoxin toxicity.

THE COMMISSIONER: Wasn't it Dr. Fowler? we have Dr. Fowler's paper that shows one case

MR. ROLAND: Q. We have Dr. Fowler's paper that shows one case, I think, in 32, in which he found a seizure - that is 3 per cent. I think his review of the literature showed a 6 per cent phenomenon for seizures.

A. I mean seizures are common in children, especially, so I don't think those figures imply any cause and effect relationship. Certainly, it is not generally accepted in any of the adverse drug reaction literature that digoxin is a cause of seizures. It may be different in very young infants, and I accept that possibility, but I don't think there are definitive data available.



K
DP/cr

1

2

3

4

5

6

7

8

9

10

11

12

13

14

15

16

17

18

19

20

21

22

23

24

25

Q. To the extent that these really are seizures in these babies then I gather that that phenomenon of seizure associated with their agonal events is a confounder. It is not one that you would expect to see from digoxin toxicity?

A. No, I could not account for it on that basis and I could not account for it just as a normal agonal event either. I think certainly incidents of that kind would be much higher than you would expect, and I believe Dr. Bain said something to that effect yesterday.

Q. So I gather then what you are saying is that there appears to be something else happening here that we don't know about?

A. I think that is a possibility. Certainly I don't think we have in hand any good explanation for the occurrence of seizures in 16 out of whatever number ---

Q. 36.

A. 26, is that the number.

MR. LAMEK: 49.

THE WITNESS: 49. That is a very high incidence of seizures. I cannot account for it on the basis of digoxin.

Q. I turn to another subject



1
2 and that is the report of Mr. Cimbura in Exhibit
3 95 and it is his report dated April 6th, 1982.
4 It is about - I don't know the sub lettering of
5 that - 95D. It is the one dated April 6th, 1982.

2
6 A. I am sorry, what page is
7 that - oh, it is 95B you said.

8 Q. 95D, D for Donald.

9 And at the bottom of that report
10 under "note" it shows that Mr. Cimbura analysed
11 specimens from four babies, Cook, Pacsai,
12 Manojlovich and Miller for alcohol and that except
13 for the Miller sample he found the presence of
14 methol alcohol and higher concentrations of ethyl
15 alcohol.

16 First of all, let us deal with
17 ethyl alcohol. As I understand it, ethyl alcohol
18 is found as one of the vehicles for IV digoxin.
19 The IV digoxin solution is about 10 per cent alcohol,
20 and I presume that is ethyl alcohol, is it?

21 A. That is correct.

22 Q. With respect to the
23 elixir of digoxin you have already told us this
24 morning that it also contains ethyl alcohol?

25 A. Yes.

Q. So I take it then we can



MacLeod, ex.
(Roland)

1

2

assume that the finding of ethyl alcohol may be explained by the fact that that is found in both IV and elixir digoxin solutions?

4

5

6

7

8

9

10

11

12

13

14

15

16

A. I think that is true in some concentrations but if you will note here, he goes on to say that he found unusually high concentrations of ethyl alcohol. He doesn't say in which samples, but then he quotes a figure of 638 milligrams per cent which I have to point out to you is in the lethal concentration range for ethanol. This is not something which is normally subject to analytical error nor is it something which appears normally as artefact and I have never seen it as an artefact in any previous report from the Centre of Forensic Sciences. Certainly it would be of interest to know why that lethal concentration of ethanol was there, and in what baby it was found.

17

18

19

20

Q. He also goes on to indicate that some of the concentrations tended to increase with time. Is ethyl alcohol a breakdown product of some other substance so that one can explain the increase?

21

22

23

24

25

A. Grapes.

Q. I am sorry?

A. Grapes, I say, sugar. No,



1

2

I am sorry, I am being - fermentation. A breakdown
of sugar.

3

4

Q. Would that explain the high
concentrations then?

5

6

A. Well, it depends on the
condition of these samples. If he is talking about
exhumed tissues, although I do not think he is in
any of these cases ---

7

8

Q. I think he is talking about
serum samples?

9

10

A. Serum samples. I don't
think that fermentation goes on in most people's
blood. The simple answer is I can't think of any
explanation for this artefactual occurrence,
especially not when you get up to that kind of
concentration. Seagram's would love to know how to
do it.

11

12

13

14

15

16

THE COMMISSIONER: I don't think
we will tell them.

17

18

Q. Let us turn to methyl
alcohol which he also finds in all of these samples
except T-29, and I gather methyl alcohol is toxic?

19

20

21

A. Methyl alcohol is a well
known poison, yes.

22

23

Q. Can you think of any

24

25



1

2

explanation, apart from artefact, for the finding
of methyl alcohol in these samples?

3

4

A. No, I cannot think of
any explanation nor can I really think how the
artefact can occur, either.

5

6

7

Q. Is methyl alcohol something
that you find around a hospital?

8

9

10

11

A. You would have 100 years
ago certainly, probably more recently than that.
This is methyl hydrate which is commonly used in
alcohol lamps. It burns very hot.

12

13

14

15

Q. Fondue pots?

A. Sterno, fondue pots. You
would not find it in the hospital I don't think
today. You might find it in the Centre of
Forensic Sciences.

16

17

18

19

Q. And I gather the finding
of methyl alcohol in blood or serum samples would
be something that would very much concern you because
of its toxic effect?

20

21

22

23

24

25

A. Yes, it depends on the
concentration. The lethal concentration range for
ethyl alcohol probably starts at about 500 milli-
grams per cent, to use the terminology he has
used here, and for methyl alcohol it is about 10



6

1

2

3

4

5

6

per cent of that so the beginning of the lethal range is 50 milligrams per cent. So it is difficult, the only concentration that we are given here is the ethanol, but that is clearly a lethal concentration.

7

8

9

10

11

12

13

I might just mention it is remotely possible, I suppose, that there is a confusion here between propylene glycol and methynol although I would not think that they should be confused in an analytical lab, but it is my understanding that Mr. Cimbura tried to explain these in the preliminary hearings and I have not read the transcript but I am told there was no explanation.

14

15

16

17

18

19

20

21

22

Q. We have talked about the possibility of errors, and we have talked about intentional administration of dosages of digoxin. Is it possible from your review of the particular babies that you have looked at that an intentional dosage of digoxin could have been given by other than an IV push, that is, could it have been given by, for instance, mixing it with normal saline in IV bags or other means like that. Is that something that is possible?

23

24

25

A. Anything is possible but I think it is very unlikely in these cases.



1

2

Q. For instance, if we look at

3

the number with respect to Cook, and I think the

4

IV bag was tested and there was not found to be any

5

digoxin, but when you look at those kinds of

6

numbers is it possible - or take the numbers in

7

Miller, post mortem are about the same as Cook, is it

8

possible to arrive at those numbers by an intentional

9

administration of digoxin through something like

10

an IV bag itself?

11

A. If you are utterly diabolical

12

there is nothing to stop you from filling up an

13

IV bag with pure digoxin solution and running it

14

in, so anything is possible. But if you are saying

15

is it possible to put one adult ampule of digoxin

16

into an intravenous bag with 250 or 500 mls of

17

fluid and then run enough of that in to produce

18

these kinds of concentrations, then that is very

19

unlikely. It is the same as the buretrol argument,

20

I think. Once you get into dilutions then you run

21

into tremendous volume problems.

22

MR. ROLAND: Thank you. Those are

23

my questions.

24

THE COMMISSIONER: Mr. Ortved, is

25

this your client?

MR. ORTVED: No, he is not, Mr.



Commissioner.

THE COMMISSIONER: Mr. Brown.

CROSS-EXAMINATION BY MR. BROWN:

Q. Dr. MacLeod, I act for Nurse Susan Nelles. There is only one area that I would like to question you on and that is with respect to Baby Cook.

You testified yesterday and you have subsequently testified to your counsel today that it is your opinion that the most likely time of administration of digoxin to Baby Cook was some time between 3:45 and 4:25 a.m. in the morning?

A. Yes, that is correct.

Q. If I understood your testimony yesterday, I believe you indicated that although it was possible that the drug could have been administered before 3:45 you considered that to be very unlikely?

A. I think if you get back before that time, I don't remember the exact context in which that was said but if you get back before that time you certainly can't account for the kinds of concentrations seen with one vial of adult strength digoxin. Perhaps that was the point. I think if you pre-supposed multiple ampules being



MacLeod, cr.ex.
(Brown)

1
2 administered then you can go back as far as you want
3 in time but you have to account for how the baby
4 survived that length of time with what would have
5 been very high concentration.

6 Q. That was precisely the
7 context in which it arose yesterday, so assuming
8 that the amount administered was only one adult
9 ampule, you would consider it very unlikely that
10 it would have been administered prior to 3:45?

11 A. That is correct.

12 Q. Again, assuming that only
13 one adult ampule was administered to this child,
14 again yesterday in your testimony in response to
15 a question posed by Mr. Lamek, he was questioning
16 you as to how long before the terminal event, or
17 the pronouncement of death at 4:56, the administration
18 could have occurred and your response I believe on
19 page 4190 of Volume 55, and in fairness the question
20 really starts on page 4188 at line 4, you stated
21 on page 4190 in response to "Yes, I'm sorry, they
22 are long":

23 "A. Rather longer than 30 minutes"
24 and I believe the 30 minutes was referring back to
25 time of death at 4:56.

"You know I would say that 30 minutes



10

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25

"is a reasonable time and that is probably a minimum time in my best judgment but it does not necessarily have to be very much longer."

Now, can I understand from that, Dr. MacLeod, that your opinion is that the likely time frame of administration was between 3:45 a.m. and 4:25 a.m. but you would be more prone to put on that spectrum the time of administration closer to 4:25 a.m. than you would be to 3:45 a.m., again assuming one adult ampule?

A. I cannot really make a judgment on that. The problem is what is represented in this figure that I drew on the board yesterday. Unfortunately, we do not know the shape of this curve, the distribution into myocardia. If we knew that it looked like this then I think we move back towards 3:45 or 3:25. If we knew that it looked like this, then it becomes possible, 10 or 15 minutes before death. We just don't have that information.

I think I would leave it within that broad range.

Q. Without a preference as to whether it was closer to 3:45 or closer to



11

1

2

to 4:25?

3

4

5

6

7

8

9

10

11

12

13

14

15

16

17

18

19

20

21

22

23

24

25

A. I could reread the whole discussion and probably give you an opinion which would be not much more than intuitive, but I think I would rather leave the broad range.

MR. BROWN: Very well. Thank you very much, Doctor.

- - - -



BmB.jc
L

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25

CROSS-EXAMINATION BY MS. FORSTER:

Q. Doctor, I take it that there is still a great deal that the medical world has to learn about the pharmacology of digoxin, is that true?

A. I think that is a fair statement.

THE COMMISSIONER: It would have shaken us if you hadn't said that.

THE WITNESS: Yes.

MS. FORSTER: Q. One of the things you still don't know is, as you just indicated to Mr. Brown, was the pattern of distribution of digoxin after an acute dose, is that correct?

A. Yes, that is correct.

Q. And I take it we do have some information about the pattern of distribution in a clinical situation?

A. Distribution into tissues?

Q. Yes.

A. Not very good information. I mean, we do have some data, particularly relating to children going to cardiac surgery where it has been possible to remove what's called the right atrial appendage, a little bit of unnecessary muscle and measure digoxin concentrations there, but in fairness,



L.2

1

2

3

4

that is not the muscle that is really of prime interest in myocardial function. So, we don't really have very usable information on this.

5

6

Q. We do have information though about the rate of digoxin going from serum to tissue in a clinical situation?

7

8

9

10

11

12

13

A. Well, we do in the sense that we have good information about the rate of its disappearance from the plasma compartment, from the circulation and of course it does go into tissues but we don't know for instance whether it goes in at the same rate into myocardium, as into skeletal muscle, as into kidney, as into liver.

14

Q. All right.

15

A. And that is trickier.

16

17

Q. And the rate of this disappearance is what you are showing on the graph that is up there now and what Dr. Spielberg showed us earlier?

18

A. Yes.

19

20

21

Q. Does that rate of disappearance, is that based on information you know about digoxin in a clinical situation?

22

23

24

25

A. Oh, yes. We have lots of data on that both from a clinical and from a more carefully controlled situation such as this Ochs paper that we



L.3

1

2

have been talking about.

3

4

Q. Do you know whether the rate of disappearance is the same in an acute situation?

5

6

7

8

9

10

11

12

13

14

15

16

17

18

19

20

Q. What I'm getting at, Doctor, is when we are going through this exercise of trying to estimate the amount of the dose and timing of a dose using the alpha and beta curves, are we really using information we know about clinical situations and trying to apply it to what may be an acute situation, an acute dosage?

21

22

23

24

25

A. Yes. Well, I mean, there are lots of precedents for doing this. I mean, the shape of that curve, the solid line now on the graph, the alpha and beta phase, the distribution curve for



L.4

1

2

3

4

5

6

7

8

9

10

11

12

13

14

15

16

17

18

19

20

21

22

23

24

25

digoxin is determined almost entirely by the circulatory state, that is, you know, the adequacy of cardiac function, how well blood is being pumped, how rapidly it is circulating and by the affinity of the drug for various tissues.

Now, clearly the latter factor doesn't likely change in a cardiac arrest per se. The former, the circulation does change and that may alter the shape of the curve and that is what I was referring to a couple of minutes ago when I said the alpha phase might be prolonged, perhaps, instead of being 20 minutes it is 40 minutes, maybe 60 minutes.

Q All right. The only point I am trying to make though is we are using what information we have about clinical situations and trying to apply it to acute situations which may be scientifically a sound analogy to make but we don't really know whether or not it is accurate at this stage of our knowledge, is that fair?

A. I guess my problem with your question is, I don't see clinical and acute as being different. You are talking about a control situation versus an acute clinical emergency and, you know, certainly we are using extrapolations there but, you know, that is not the kind of extrapolation that



L.5

1

2

clinical pharmacologists are unhappy with and that
is partly what our business is.

3

4

5

6

7

8

Q. I take it as well, Doctor,
when we were going through this exercise of trying
to estimate the size of the dose and the time of
the dose is, you indicated to Mr. Lamek yesterday
you could get a variety of different answers
depending on what point in the alpha curve you pick?

9

10

11

12

A. That is correct.

13

14

15

16

17

18

19

20

21

22

23

24

25

Q. And it really boils down to
estimating a range of doses and times that are
reasonably possible?

A. Yes. You really are trying
to discern several unknowns from one known and in
honesty it ain't possible.

Q. I take it though it is possible
to rule out some scenarios as being so unlikely that
we don't really have to entertain them, such as, if
you had a child who had never been prescribed
digoxin and you found post mortem both levels in the
serum and in the fresh tissue you could rule out with
a fair degree of certainty the possibility that the
level was taken right at the point of administration
because we know there is digoxin in tissue?

A. Yes, although, you know, I got



L.6

1

2

3

4

5

6

7

8

9

10

11

12

13

14

15

16

17

18

19

20

21

22

23

24

25

into this discussion with Mr. Lamek yesterday,
because we don't know the shape of that distribution
curve into tissue, it may be that the drug appears
there very, very early on in its circulation. I
said five seconds which is really taking a ridiculous
extreme but, say, a couple of minutes, it is quite
possible.

Q. Sure.

A. There are many drugs that
appear in the liver in very high concentrations within
a couple of minutes.

Q. And that would serve to even,
if the curve was steeper, that would serve to even
broaden the range of possible doses and possible times?

A. Yes.

Q. All right.

A. That is correct.

Q. And in some cases I take it
we are able to rule out administration more than two
and a half hours prior to death because of the sheer
number of ampules that would have to be administered
to a child in order to achieve a level?

A. Yes, I think at some point it
becomes just impossible to put particular volume into
a child of a certain size. So, I think you are right,



L.7

1

2

within broad limits we can rule out some of those possibilities.

3

4

5

6

7

Q. And between, leaving aside the broad limits, when we are left with a range of possibilities, the best you are able to do is give us your educated guess as to what might be most likely?

8

9

A. Absolutely.

10

MS. FORSTER: I wonder if this might be a convenient time, Mr. Commissioner?

11

12

THE COMMISSIONER: Yes. all right.
Yes, Mr. Young.

13

14

15

16

17

MR. YOUNG: Mr. Commissioner, I apologize for being late this morning but I have since been informed that we are to have a meeting at 3:30 this afternoon and I have spoken with Mr. Percival and of course we will be in attendance at that meeting.

18

19

20

21

22

23

24

25

With respect to the potential of having the argument later this afternoon as originally planned, might I say that we have stopped our research and I just spoke to Mr. Percival and he is shelving it until tomorrow and Monday and we will be prepared on Tuesday but we would like some assurance that we will not be called on later this afternoon to argue



L.8

1

2

now that we have been told that we likely won't be
asked to argue.

3

4

THE COMMISSIONER: Yes, all right.

5

MR. YOUNG: Do I have that assurance?

6

7

THE COMMISSIONER: Well, it is an
ill wind that blows nobody good. All right. Well,
that's fine, we won't do that but we will have the
meeting. The object of the meeting is to see if we
can resolve this police report problem and if we can
resolve it then it becomes entirely academic.

8

9

10

11

MR. YOUNG: And I hope we can at that
time, sir.

12

13

14

15

16

THE COMMISSIONER: And if we can't
resolve it I am hoping that we will get on with that
matter on Tuesday after I have delivered myself of a
judgment on the other two issues so that everybody
will know where they stand on those two.

17

18

19

MR. YOUNG: And if it is still
necessary to argue the police report we will be here
and prepared to do so.

20

21

22

THE COMMISSIONER: Yes, all right,
thank you. I wonder if we could just take another
poll, I want to see how we are.

23

24

25

Mr. Hunt, how long - well, how long
will you be, Miss Forster?

L.9

1

2

MS. FORSTER: My best guess is about
20 minutes, sir.

4

THE COMMISSIONER: Mr. Hunt?

5

MR. HUNT: I won't be that long, 15
minutes, sir.

6

7

THE COMMISSIONER: Mr. Young?

8

MR. YOUNG: I would expect 10 or 15
minutes, Mr. Commissioner.

9

10

THE COMMISSIONER: Miss McIntyre?

11

MS. KITELY: It is Kitley, sir.

12

THE COMMISSIONER: Yes, Kitley.

13

MS. KITELY: 10 or 15 minutes, sir.

14

THE COMMISSIONER: Mr. Knazan?

15

MR. KNAZAN: I may be a half an hour.

16

THE COMMISSIONER: We are going to
be in trouble.

17

MR. OLAH: 15 to 20 minutes, Mr.
Commissioner.

18

THE COMMISSIONER: Mr. Labow?

19

MR. LABOW: I will also be 15 or 20
minutes, Mr. Commissioner.

20

21

THE COMMISSIONER: Mr. Tobias?

22

MR. TOBIAS: Well, Mr. Commissioner,
I have to help you out, I will be about five minutes.

23

24

THE COMMISSIONER: Well, I will give

25



L.10

1

2

you another credit, I guess. Well, I think we will
be back here at 2:15 I think and we will see what we
can do.

4

5

--- Luncheon recess

6

7

8

9

10

11

12

13

14

15

16

17

18

19

20

21

22

23

24

25



AA/DM/ak

1

2

---Upon resuming at 2:30 p.m.

3

THE COMMISSIONER: Yes, Miss Forster.

4

MS. FORSTER: Thank you, sir.

5

6

7

8

9

Q. Dr. MacLeod, dealing now with the case of Justin Cook. I believe you told us that your best estimate as to the timing of the dosage was the administration of one adult ampule or slightly less, some time between 3:45 and 4:25 in the morning.

10

11

12

13

14

15

A. I don't believe I speculated as to the number of ampules, but if you take as an assumption that it is more likely to be one adult ampule or less, then those are the correct times. I mean, I have no way of knowing at all whether somebody perhaps administered several ampules at an earlier time.

16

17

18

19

20

21

Q. Actually that is what I wanted to get at, Dr. MacLeod. What factors did you consider then in arriving at your appropriate timing, if you were not starting with the assumption of given a dose of one ampule the timing would have to be 3:45 to 4:25, how are you arriving at your estimate of the timing?

22

23

24

25

A. No, I think you have set certain conditions. If you leave it wide open there could be several ampules; and accepting perhaps that he survived



AA2

1

2

3

4

5

6

7

8

9

10

11

12

13

14

15

16

17

18

19

20

21

22

23

24

25

without any obvious consequences of that overdose for a period of time, then the time can be moved back earlier. I think, I'm not sure whether I set the conditions or Mr. Lamek set them, I rather think Mr. Lamek set them, but within those conditions one adult ampule or less I would think that time range is reasonable.

Q. So you think given a specific dose, this is the time; and similarly if you were given a smaller dose you would come up with the time perhaps closer to death, and a larger dose time further away.

A. Yes. I think you have to set some of those variables but you don't know any of them. The only thing you know for sure is the concentration at the time of death, or shortly after.

Q. Thank you. Now, Mr. Lamek reviewed with you yesterday the possibility of confusing digoxin with some of the other drugs that were administered to this child. I don't believe he reviewed with you one drug that was given to the child, and that was adrenalin which was given during the resuscitation efforts. I take it adrenalin was most certainly found on crash carts in 1981.

A. Oh, yes, adrenalin is a



AA3

1

2

standard crash cart medication.

3

4

As I understand it the vials of
adrenalin are clear glass similar to vials of
digoxin?

5

6

A. Yes, in my experience they have
always been clear glass.

7

8

Q. The adrenalin itself was a
clear colourless liquid similar to digoxin?

9

10

A. Yes, it is.

11

12

13

Q. Dr. Spielberg told us that in
1981 when administering adrenalin it was necessary to
draw up the adrenalin and dilute it, is that your
understanding?

14

15

16

17

18

19

A. I am not sure he is correct in
that. I would have to check on the exact time when
we changed; but some time after 1979, which is when
I started at the Hospital for Sick Children, several
products were introduced in pre-filled syringes,
particularly for this emergency type of medication
and I am virtually certain adrenalin is one of them.

20

21

22

23

Q. He did indicate that one of
the reasons that adrenalin was not pre-loaded was
because of the ease with which one could make a
mistake in administering it.

24

25

A. No question about that. I



1
2 think that was probably introduced before March of
3 1981.

4 Q. Doctor, if it is necessary for
5 you to come back here another day, would you mind
6 advising me as to when in fact pre-loaded adrenalin
7 was introduced into the Hospital?

8 A. Yes. I think that information
9 could probably be obtained from the minutes of the
10 Pharmacy and Therapeutics Committee, and maybe
11 Mr. Batty could find the information for you.

12 Q. Fine, thank you.

13 A. I shouldn't be volunteering his
14 services.

15 THE COMMISSIONER: I would much rather
16 volunteer his services than have you come back.

17 MR. LAMEK: Mr. Commissioner, maybe
18 we can resolve the thing without putting Dr. MacLeod
19 to that effort. Volume 22 of the evidence at
20 the preliminary hearing; Dr. Jedeikin who I understand
21 was present at the Cook arrest said:

22 "They were drawing up the calcium
23 bicarbonate and adrenalin are usually
24 in already assembled arrest vials. All
25 one does is break off the needle, or
even use the needle and inject it



AA5

1

2

"directly into the intravenous tube."

3

So apparently a pre-packaged syringe was essentially
4 in use at that time.

5

THE WITNESS: That is what my
6 recollection is.

7

MS. FORSTER: I'm sorry,
8 Mr. Lamek. Did you say his evidence was they were
9 in vials?

10

MR. LAMEK: In already assembled
10 arrest vials but they have a needle on it, he says:

11

"They are adrenalin vials that one
12 can open by usually in this situation
13 we use these pre-mixed pre-designated
14 dosage vials."

15

THE WITNESS: Vial is probably not
15 the right word for that.

16

MR. LAMEK: Yes.

17

THE WITNESS: It is a pre-loaded
18 syringe much like what we use nowadays.

19

MR. OLAH: Dr. Costigan offered some
20 evidence in that regard but he could not recall
21 specifically what was pre-loaded?

22

THE WITNESS: Yes, at that time and
22 even now there are some things that are in syringes
23 and some things that are not, it is partly a question
24

25



A6

1

2

of what the pharmacy is willing to prepare in advance.

3

4

5

6

Q. Were there normal glass ampules and vials of adrenalin still available on the wards after the introduction of the pre-loaded vials or syringes?

7

8

9

10

A. I am really not in a position to answer that. I imagine that they were in some places. Certainly - the pre-filled syringes to my recollection were introduced primarily on the crash cart.

11

12

13

14

15

16

Q. Now, when you discussed the case of Allana Miller with Mr. Lamek, Dr. MacLeod, you indicated that this was a case where you felt it was not even legitimate to speculate as to the timing or amount of the dose the child received. Could you tell me why in this case you felt it was not legitimate to speculate?

17

18

19

20

21

22

23

24

25

A. Well, it is the same problem that we have with all of the cases. You have one isolated measurement, a serum concentration or a tissue concentration, not really a serum concentration. When that is your only information it is impossible I think to draw any conclusions about the magnitude of the dose or the time of the dose relative to the actual measurement; that is the elapsed time between



AA7

1

2

dose and measurement. You are trying to discern two
variables knowing one, knowing one out of three.

4

Q. What separates this case from
some of the cases where you have estimated?

6

A. Well, I think in Pacsai's case,
I'm sorry, not Pacsai.

7

8

Q. Cook.

9

A. The Cook case you have got quite
a different situation. You have a child who is not
receiving digoxin, so you can't presume, given our
information about medication errors, I think you
can presume that you are starting from zero. You have
a tissue concentration on a fresh specimen that is
taken immediately at death. So you have got quite
a bit more information to work with there and that
is what allows you to speculate.

10

11

12

13

14

15

16

17

Q. Thank you. Now going to the
Pacsai case, I believe you told Mr. Lamek that the
digoxin levels in this child could be attributable
either to an unprescribed dose of digoxin, or to some
pathophysiological change, is that correct?

18

19

20

21

A. Yes.

22

23

Q. And you told Mr. Lamek as well,
as I understood it, that you favoured the scenario
of an oral dose given some time prior to 5:30 a.m.

24

25



1

2

3

4

A. Yes, that seems to me the most likely explanation. I believe I used a split of 75/25, it is quite arbitrary and ---

5

6

7

8

9

10

11

Q. Dealing with the scenario of the unprescribed dose of digoxin only and not with the pathophysiological changes for a moment, you indicated as I understand it to Mr. Lamek that if that was the case it was - you favoured the assumption of an oral dose prior to 5:30 a.m.

12

13

14

15

A. Yes, I think that would be more compatible with the clinical course.

16

17

18

19

20

21

22

A. Well, that won't explain all of the levels. Maybe I can draw a picture just so you get some idea of the uncertainty and I'm really not trying to confuse the issue. I guess we shouldn't over-simplify our assumptions. It's just possible, if you are looking at Pacsai, that say a relatively small IV dose was given, I have to get my time straight here, shortly before 5:30.

23

24

25

Q. Just prior to going to the ICU.

A. Let us say this is a fairly



1
2 rapid IV administration of 20 micrograms of digoxin,
3 or 30 micrograms of digoxin, not a huge dose, you
4 might get a peak of say 25 nanograms per ml and then
5 you get into your alpha phase; and you know, this is
6 the time when Costigan is seeing him and he is
7 transferred to ICU perhaps here; and this is I guess
8 at something like 6:15 or 6 o'clock. At that point
9 we are told that the level is 10 nanograms per ml.

10 Then maybe the curve continues to
11 come down, I'm sorry I didn't mean to put a bump in
12 there, down to a steady state concentration, and
13 maybe - and this is the time in ICU. Maybe for the
14 sake of argument one could say another dose is given
15 in the ICU that was the question I believe that
16 Mr. Roland put to me. So you go back up again, you
17 are into another phase, and this is perhaps the time
18 when death occurs which is the arrest at 8:15 and
19 death is 8:45.

18 Q. No, 8:45 was the arrest.

19 A. I think he was declared dead
20 at 8:45.

21 MR. LAMEK: No, 10 o'clock.

22 THE WITNESS: I am confusing you then.
23 Let us say we are now up to 10 o'clock, time of death,
24 and then you get the post mortem multiplier effect,
25



1
2 and you get a reading of 26, but you are not
3 necessarily - you know, we are all assuming that the
4 10 measured back here at 6:15 has to be related in
5 some way to death, there is nothing about that that
6 tells you there was no dose given in this intervening
7 period, that is the only point I was trying to make.

8 Q. The 10 I take it can be
9 related to a post mortem level of 26 however.

10 A. It would make some sense if that
11 is the case, but you can't, we don't know for instance
12 if that is the steady state concentration.

13 Q. That's right.

14 A. Assuming that it is in the
15 distribution phase of some kind, it is quite likely it
16 came down further during the period in ICU, and where
17 it would bottom out depends on the absolute magnitude
18 of the dose. It wouldn't be unreasonable to expect
19 to see it bottom out at something like 5, it would
20 still be compatible with 4 or 5 whole multiplier
21 with a post mortem level of 26. It is quite within
22 the realm of possibility that another dose oral or
23 intravenous was given during that time in ICU. I
24 wouldn't think a big dose, but perhaps a therapeutic
25 dose or a slightly higher than therapeutic dose.

Q. I take it is also within the



1
2 realm of possibility that there was one single dose
3 given when the child was in the ICU.

4 A. No, I don't believe I suggested
5 that, you still have to account for the level of 10.
6 I'm sorry, what you are suggesting is correct, providing
7 you will accept the pathophysiology argument that maybe
8 the level of 10 at 6:00 or 6:15 can be accounted
9 for by the high potassium displacing dig. from other
10 tissues and that is a possibility.

11
12
13
14
15 -----
16
17
18
19
20
21
22
23
24
25



BB
DP/cr

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25

Q. Dr. Spielberg told us when he was looking at this child that one of the enigmas that he faced in interpreting the levels of 10 and 26 was the fact that the child returned to sinus rhythm when he was in ICU. He had difficulty with this.

I want to ask you first of all whether or not you considered that fact when you were estimating your dosages and your timing, and what significance you gave it?

A. I am aware of that fact. I have not got the chart in front of me any longer. I am not certain that he returned to sinus rhythm for any very long period. Certainly his cardiac rhythm was changing throughout this period. This is not unusual in cardiac rhythm disturbances.

Q. If I can assist you, Dr. MacLeod, it is found at page 101 of the Medical Record of Kevin Pacsai. In the discharge report prepared by Michael Schaffer, in the second last paragraph it says:

"In the Intensive Care Unit, the child was noted to be back in sinus rhythm."

A. Yes.



1

2

2

Q. My question simply is,

3

if the child received an overdose of digoxin prior
to admission to the ICU, would you expect a return
to normal sinus rhythm?

5

6

A. I think that is possible,

7

yes. Again, maybe it suggests this scenario, that
what you are really seeing, maybe the level of 10
at 600 is a distribution phase artefact, if you
want to call it that. That is, it is a high value
but does not necessarily mean high values in tissue.
It then goes down to five and it otherwise is well
and then there is another dose given or something
else happens and this triggers off the terminal
event. I think that is possible.

10

11

12

13

14

15

16

17

To be honest with you, it is not
completely impossible for somebody in the throes
of digitalis toxicity to have periods of normal
cardiac rhythm.

18

19

20

21

22

It would be nice to have something
more than a note in a discharge summary saying
that that happened. Is there actually documentation
of that in the clinical record, because I certainly
did not have that impression.

23

24

25

THE COMMISSIONER: I thought we
had some trouble with that one, did we not?



1
2 MS. FORSTER: Yes, sir. The only
3 other reference I found is on page 66, the ICU
4 note prepared by Dr. Costigan indicates the child
5 was:

6 "Transferred to ICU. On leaving
7 ward developed brady 40, cyanosis
8 and brief apnea. Responded to
9 stimulation."

10 I am not sure that Dr. Spielberg
11 could point us to any reference other than the
12 reference on page 101 that I directed you to.

13 THE WITNESS: One has the impression
14 from reading Costigan's note that this child had
15 very unstable cardiac rhythm that was alternating
16 from 2 to 1 block, 3 to 1 block, sinus bradycardia,
17 sinus tachycardia I think even at some point. So
18 it is really not surprising if heart rhythm is
19 changing that there might be periods of what would
20 be considered normal in sinus rhythm. That probably
21 would be compatible with the underlying cardiac
22 conduction problem.

23 Q. Looking again at the range
24 of possibilities in terms of timing and dosage,
25 is it conceivable that the child could have received
the overdose of digoxin, if it received an overdose



1

2

of digoxin, as much as 11 hours prior to death, and
still achieve these levels?

3

4

A. Again, anything is possible.

5

I think it is pretty unlikely, given this particular
child and given the descriptions of him as being
fairly normal through the night.

6

7

8

Q. Are you able to give us
any kind of estimate as to the kind of dosage he
would have to receive 11 hours prior to death to
have these levels?

9

10

11

A. I think it is difficult to
speculate on that, again because of his underlying
condition. I mean even that is in dispute, I guess,
but assuming that he has an underlying condition
that predisposes him to hyperkalemia, to high
potassium, it may well be that the binding of
digoxin to his tissues will be different from the
binding in normal individuals or in other children,
even other children with heart disease, so it is
possible that a level of 10 in Kevin Pacsai does
not mean the same as a level of 10 in some other
child. Normally you would say that if 10 was a
steady state of digoxin concentration that really
would only be compatible with quite a large oral dose

12

13

14

15

16

17

18

19

20

21

22

23

24

25



1
2 and thus it would be unlikely that he would survive
3 through 12 hours after it. However, if the other
4 things are different then perhaps a lower oral dose
5 could be postulated and that might change things,
6 but we are really off into the realm of wild
7 speculation, I think.

8 Q. Doctor, I take it that
9 you co-authored Appendix 2 of Dr. Bain's report,
10 with Dr. Spielberg?

11 A. Yes, that is correct.

12 Q. Have you had an opportunity
13 to review that appendix recently?

14 A. To be honest with you I
15 have not read it in about a year but I have
16 probably got it here. Maybe I did not even bring
17 it. I guess it is in my case. I have a copy of
18 it.

19 Q. I take it it was prepared
20 some time around the summer of 1982?

21 A. It would have been prepared
22 in late June, early July, 1982.

23 Q. I just had one simple
24 question for you regarding this. I don't know if
25 you can answer it as you have not read it recently,
but I just wonder whether any of the conclusions



1

2

that you have expressed in that appendix have changed
or whether you still hold to them today?

3

4

A. I better look and see what
the conclusions were, should I not?

5

6

6

THE COMMISSIONER: Unfortunately
there is no heading marked "Conclusions". Were
you referring to the recommendations or were you
referring to the whole report?

7

8

9

MS. FORSTER: No, the explanations
for how the levels occurred, basically.

10

11

12

13

14

15

16

17

18

19

20

THE WITNESS: I don't think this
report as I recall really explains in any detail
how levels occurred. What it was intended to do
was to point out a number of doubts that should exist
in the minds of those looking at these levels and
trying to interpret them. I guess it goes without
saying that we felt that the interpretation that
was presented at the preliminary hearing was really
pretty simplistic and did not take into account
many of the variables that you have since heard about
from Dr. Spielberg and others.

21

22

23

24

25

Q. I take it one further
variable that perhaps was not in existence at the
time this appendix was prepared was that expressed
by Dr. Kauffman at the Gary Murphy inquest dealing



1

2

with the physiological changes that can account
for elevated levels?

3

7

4

A. You mean we were unaware of
Dr. Kauffman's views or ---

5

6

Q. It is not really discussed
in this appendix.

7

8

A. Well, no, I think at this
time we really were not attempting to explain these
on a case by case basis.

9

10

11

12

Q. I understand that, but
surely would that not raise another doubt in your
mind in terms of raising possible hypotheses as to
how the levels were there?

13

14

15

16

17

18

19

20

21

22

23

24

25

A. Oh, yes. Our own thinking
about this has evolved since that time. I don't
think there have been really vast amounts of
new information that have come to light that have
changed our thinking. I think had we sat down and
gone through case by case at that time we would have
said very much the same sort of things that we say
now, and Dr. Spielberg and I would probably have
the same minor differences of opinion, and Dr.
Kauffman will have some more differences of opinion.
But I have read this report in the last six months
and I am not going to read it word for word right



1

2

now, but I imagine it represents fairly the way

3

we feel today.

4

Q. Doctor, finally, are you

5

familiar with the way in which the medication rooms

6

on the wards were set up in 1980-1981?

7

A. In a general sense only.

8

They differed from ward to ward.

8

9

Q. Are you in a position to

10

describe to me the set up of the medication rooms

in 4A and 4B?

11

A. I think you should put that

12

question to the pharmacist who was assigned full time

13

to that ward.

14

MS. FORSTER: Thank you, Doctor.

15

THE COMMISSIONER: Thank you, Miss

Forster. Mr. Hunt.

16

17

18

19

- - - -

20

21

22

23

24

25



BmB.jc
CC

1

2

CROSS-EXAMINATION BY MR. HUNT:

3

4

5

6

7

8

9

10

11

12

Q. Doctor, my name is Hunt and I represent the Attorney General and the Coroners in related interests. I would like to deal firstly with your evidence of yesterday with respect to Justin Cook and if I could summarize it for the purpose of giving you the background to my question I would ask you to bear in mind that I am trying to summarize it and if you don't agree with me just say so. But I take it from your evidence that in respect of Justin Cook you are satisfied that he got a dose of digoxin beyond question?

13

A. Yes, I can accept that.

14

15

Q. That you are of the opinion that the dose would have been a deliberate dose?

16

17

18

A. Well, I think by inference it probably is in that I couldn't see any clear place in his treatment where a medication error could have occurred.

19

Q. Right.

20

21

A. But I don't think I said specifically that I felt it was a deliberate dose.

22

23

24

25

Q. All right. I think the words you used was that you imagined it was a deliberate dose?



CC.2

1

2

3

4

5

6

7

8

9

10

11

12

13

14

15

16

17

18

19

20

21

22

23

24

25

A. Well, I think the probability is that it was.

Q. All right. And you said that it probably caused his death but that you couldn't say for sure. Now, am I correct that Justin Cook was a baby who was not on digoxin and in fact at that point in time it was contra-indicated, I think were the words Dr. Freedom used.

A. Yes.

Q. He no doubt was a sick, very sick child or he wouldn't have been in the situation that he was in at that point in time. Am I also correct that digoxin in a large enough dose would on anybody have the effect of really causing the heart to simply stop pumping?

A. You know, there is an old saying in pharmacology that enough of anything will do anything. But I think if you are thinking of it stopping dead in its tracks, you know ---

Q. No, I'm not suggesting you stop it dead in its tracks but ultimately the effect of digoxin is to stop the heart from pumping.

A. Well, I mean, everybody dies of cardiac arrest, you know, eventually.

Q. Well, digoxin has a direct



CC.3

1

2

effect on the heart in that respect, does it not?

3

4

5

6

7

8

9

10

11

12

13

14

15

16

17

18

19

20

21

22

23

24

25

A. Yes. Well, it does different things. I mean, it interferes with conduction and, I mean, that may be a block, the kind of thing we are talking about Pacsai where, you know, there is an atrial tachycardia with a block at the nodal level. The other thing it does is, it increases automatisity. That is probably the major toxicity in a high dose. Increased automatisity, that means the heart starts to beat spontaneously, other pacemakers get set up. Instead of following the normal course of conduction from the sinus node to the AV node to the ventricular muscle you get foci developing within the ventricle itself, within the ventricular muscle. These things just discharge spontaneously and that is what sets off what is called ventricular fibrillation. Once you develop ventricular fibrillation you have got no effect of pumping action.

Q. All right.

A. And then the heart dies or the patient dies.

Q. All right. So, it may be that there is a chain of reactions that it sets off but the ultimate effect of it, because of its direct effect on the heart is that the heart simply stops?



CC.4

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25

A. I guess I am just quibbling over the word "stops". It doesn't just stop. You stop getting enough oxygen to the heart and then it eventually stops.

Q. All right. That is part of the chain of reactions that lead to that event?

A. Yes.

Q. All right. Well, I guess my concern I had about your evidence is that inasmuch as we are satisfied that he got a dose of it, that it has this effect in a large enough dose of ultimately leading to a chain of reactions that bring about the ceasing or functioning of the heart, why is it that you are so cautious in respect of cause of death that you will say only that it is probable that it had the effect of bringing about his death?

A. Well, I think you misunderstood me. The question is, you know, has cause and effect been shown and the answer is no, it hasn't been shown, it can't be shown.

Q. Right.

A. I don't doubt that if that level of digoxin was present long enough that it would eventually kill this child.

Q. All right.



CC.5

1

2

3

4

5

6

7

8

9

10

11

12

13

14

15

16

17

18

19

20

21

22

23

24

25

A. The question though did it kill him, it might have been given five seconds before he died and he might have died of something else. I think I used the analogy later on, or maybe it was this morning, to this case in Edmonton with the morphine in the newborn where a great deal of time, several weeks was spent discussing whether the baby died before the morphine given in overdose had a chance to kill him. It is really the same situation. Maybe I am quibbling needlessly, I don't think it is an important point, I just don't think you should just assume a priori that a high concentration means that that was the cause of death, it doesn't, it's not proven.

Q. I suppose, and that perhaps clears it up but I suppose just looking at it from the point of view of a layman and seeing certain circumstances demonstrated such as the administration of a high amount of a drug that has a direct effect on the heart that leads to its stoppage putting the factors together to my mind would seem to suggest to me that one could say with reasonable degree of certainty that there you have it.

A. Well, I have to disagree. I mean, that would be true if it happened to you, I



CC.6

1

2

3

4

5

6

7

8

9

10

11

12

13

14

15

16

17

18

19

20

21

22

23

24

25

assume, in the next half hour but it isn't true if it happens to somebody like Justin Cook who has already had episodes of near death who has got a very severely deranged heart structurally and who is susceptible to sudden death. All I am saying is that lightning may have struck him before the digoxin did.

Q. It would be an extreme coincidence if he died simply of the normal deterioration of his heart through his disease while coincidentally he had this high level of digoxin floating through his system and in his tissues?

A. I agree it would be a considerable coincidence.

Q. Okay. And it may be I suppose that if digoxin were administered in this high level it might have an effect on the heart that before the digoxin had its complete effect it could cause the heart to simply deteriorate faster than it otherwise might and bring about death as a result of something that was more specifically related to the disease of the heart than to the digoxin, would that be possible?

A. I am really not sure that I follow your question but I think what you are following up on is the statement that digoxin is contra-indicated



CC.7

1

2

in this kind of child anyway.

3

4

5

6

Q That's true, it could make things worse and kill him before it got to the point where it itself had the effect of setting in an action, reactions that would bring about the stopping.

7

8

THE COMMISSIONER: It would become a delicate question under those circumstances whether the digoxin killed him or not.

9

10

11

12

MR. HUNT: No question. The bottom line is, in those circumstances certainly one would have to say it is a contributing factor, in fact, accelerates the death of the child.

13

14

15

16

17

18

19

20

21

THE WITNESS: Oh, yes. I don't think there is any question that digoxin would have had an adverse effect on this child and more digoxin would have had a more adverse effect. But it is not an "all or nothing" phenomenon and when they say that digoxin is contra-indicated that's on a somewhat theoretical basis in that the heart is pumping harder it may in fact get less blood out, so, working harder for less pumping and, you know, whether that would actually happen in this child at that time ...

22

23

24

25

THE COMMISSIONER: Well, if this question could be put to you, and Pacsai may not be the best example, but if nothing else, if his heart,



CC.8

1

2

his heart ailment had not killed him, would the

3

digoxin have killed him?

4

THE WITNESS: Cook you are referring
to, are you?

5

6

THE COMMISSIONER: Well, are we in
Cook now?

7

8

MR. HUNT: Yes, we are dealing with
Cook.

9

10

11

12

13

14

15

THE WITNESS: We are talking about
Cook. Well, yes, assuming that we had an overdose
of at least one adult ampule, 500 micrograms of
digoxin, I think probably it would have, although,
you have to qualify that to say that there are a
number of survivors with quite high concentrations
and children as well as adults who have normal hearts.

16

THE COMMISSIONER: Well, we have
never seen anyone survive I don't think with this.

17

18

THE WITNESS: Well, there are
survivors of 30.

19

THE COMMISSIONER: Yes.

20

21

22

THE WITNESS: And there certainly are
survivors for several hours at 200 but I think, you
know, with a high degree of probability it would
cause death even with a normal heart.

23

24

MR. HUNT: All right.

25



CC.9

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25

Q. Now, dealing with the time frame that we have been concerned with, and again this is with respect to Justin Cook of 3:45 to 4:26, if we are satisfied that Justin Cook received an overdose of digoxin and that the ultimate arrest that led to the resuscitation efforts was as a result of that overdose, is it fair for us to take into account in examining that period the, albeit brief period before the immediate arrest where we start to see some sort of distress that he is into, which leads to the calling of the Code 23, for example, and the administration of the propranolol, prior to that to an attempt to rectify the situation, is it fair for us to really look at this and take into account that whole sequence of events and the situation that he was in immediately prior to the arrest?

A. Well, I think all of those events fall within that broad time frame.

Q. Yes, they do.

A. That I have suggested.

Q. That's right. And you have suggested that we can go back to 3:45 in terms of the time at which it is likely the dose was administered?

A. Yes, I think that is the earlier time.



CC.10

1

2

Q. Sure.

3

A. I haven't got the chart again

4

but I think 3:25 is the time at which the resident

5

was first called because of the tet spell.

6

Q. I'm sorry, it was at 3:45.

7

A. I'm sorry, 3:45, yes.

8

Q. What I am suggesting though is

9

that inasmuch as that is really all part of it, in

10

examining this question of the administration of the

11

dose, is it fair for us to consider that what we

12

see happening in terms of the distress that led to

13

the calling of the Code 23 and then the Code 25 came

after the administration of the dose?

14

A. Yes, I think that is probable.

It may have, shortly after.

15

Q. Well, we are not dealing with

16

the time yet because as I understand it the reaction

17

to a dose of digoxin can happen very quickly,

18

depending upon the condition of the child and the

19

amount of the digoxin that was given?

20

A. This is correct.

21

Q. And that could be I suppose

22

within a matter of a few minutes, 10 minutes, something

as short as that?

23

A. Yes.

24

25



CC.11

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25

Q. So that in terms of sort of looking at the question of the timing of the dose, if you use 3:45 as the start of the distress then we are really sort of forced to look at the period immediately before that as a period when it was likely given?

A. Oh, no, I don't think that necessarily follows at all. I mean, you have a child here who was subject to sudden spells of reduced cardiac output, a so-called tet spell and had had one of these the night before and to my knowledge nobody has suggested he was given digoxin the night before.

Q. Oh, no.

A. Well, why do you need to postulate some other event to cause this spell at 3:45?

Q. Well, we ---

A. It appeared to everybody who dealt with him that it was a typical tet spell.

Q. It would be a remarkable coincidence if at 3:45 through simple normal deterioration of his condition he had one of these spells and at the same time had a huge dose of digoxin in his system, would it not?

A. No, I don't find that a remarkable coincidence at all. I mean, I think we have



CC.12

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25

already discussed this morning the possibility, perhaps the syringe that was taped to his bed that contained, ostensibly contained propranolol solution, perhaps it contained digoxin. So, maybe the person, the physician who thought he was treating the tet spell was in fact administering digoxin, that is perfectly possible.

Q. Well, that may be, but I thought that sort of in going through your analysis of it you had left us with the position that while anything is possible it seemed rather unlikely that that is how the digoxin got into his system?

A. No, not at all, quite the opposite. I said I thought it was unlikely that somebody drawing up propranolol into a syringe, and I believe the circumstances were that they went to another ward to obtain the propranolol and drew it up, I thought it was unlikely that somebody would take propranolol for digoxin, or mistake digoxin for propranolol to be correct, and the reason I said that is that one is in a coloured ampule and one is in a clearer ampule, one is a 2 ml and one is a 1 ml ampule and I just don't think that that combination of mistakes would likely be made under those circumstances.



CC.13

1

2

3

4

5

6

7

8

9

10

11

12

13

14

15

16

17

18

19

20

21

22

23

24

25

However, Mr. Roland asked me subsequently whether I thought that it was possible that there was digoxin in that syringe and I said certainly that would correspond exactly.

Q. So, on the one hand you are dealing with medication error resulting in digoxin getting in the syringe; on the other hand, the proposition is put to you that perhaps somebody put digoxin in the syringe purposely and left it there so that it ultimately would get administered?

A. Yes, absolutely, or alternatively, that in the confusion of treating a bona fide tet spell at 3:45 in the morning somebody seizes the opportunity to administer digoxin. I mean, that is perfectly feasible.

Q. Okay. Well, let's leave just for the moment that second proposition aside that somebody put it in the syringe intentionally to have it administered later. If we just assume that that is not the case, then aren't we looking at really the onset of those distressful events at 3:45 as being the start of the period where we have to consider that perhaps this is a reaction to the dose of digoxin having been administered?

A. Oh, you have to consider that,



CC.14

1

2

3

4

5

6

7

8

9

10

11

12

13

14

15

16

17

18

19

20

21

22

23

24

25

but I suggest to you that it is at least an equal
probability that those events at 3:45 were due to
the patient's natural condition.



DD/DM/ak

1

2

3

4

5

6

7

8

9

10

11

12

13

14

15

16

17

18

19

20

21

22

23

24

25

Q. But we have to account for the digoxin at some point, so I am just trying to narrow down the avenues that are open to you.

A. I have given you a broad range, I think 3:45 is probably the earliest at which you could account for it; and so more likely it is a little later and if you accept that view then you accept that the sequence of events at 3:45 was really a tet spell.

Q. Sure. But the sequence of events at 3:45 are really the start of the distress that the digoxin is causing, then the period we are concerned with is 3:45 or immediately before that?

A. Not necessarily immediately before, you may go back even further.

Q. But we are dealing here with the hypothesis of one adult ampule.

A. Then you are in trouble I think.

Q. How?

A. Because I think you cannot expect to postulate one adult vial given prior to 3:45 and still explain a level that is only, I am sorry, and still explain a level of 74 whatever it is, an hour and a half later.

Q. But you can explain it if it is



DD2

1

2

given at 3:45?

3

A. Well, there is some critical

4

point and there are a number of unknowns in here.

5

Q. Right.

6

A. Mr. Lamek eventually pinned

7

me down to 3:45 by working me back to the bare

8

minimum, and now you want to work me back to ---

9

Q. No, I just want to draw your

10

attention, sir, if what we are dealing with when

11

these events begin at 3:45 is really the reaction,

12

the beginning of the baby's reaction to the digoxin,

13

then we obviously have a situation where sometime

14

however short a time before 3:45 the digoxin went

15

into the baby's system. I am not trying to take you

16

back to any length of time, it may be as much as one

minute before 3:45, or 2 minutes.

17

A. But you are taking me back

18

further, because in fact it is not likely that the

onset is that rapid.

19

Q. All right.

20

A. And I believe there was an

21

initial favourable response here, for example, and

22

again I haven't got the chart in front of me, but I

23

think it was atropine, it is described as giving a

24

favourable response. You know, we are not seeing

25



1

2

D3

3

4

5

6

an inexorable downhill course starting at 3:45. It seems much more likely to me that what you're seeing there is normal manifestation of this child's heart disease and that the trouble related to digoxin, if it occurs at all, occurs some time later than that.

7

8

9

Q. Well, I am just looking at the note on the chart which is Exhibit 116, page 29, it is Nurse Nelles' notes of the events beginning at 3:45. I don't know if that is the one.

10

11

A. I haven't got the chart.

12

THE COMMISSIONER: And the page?

13

Mr. Commissioner.

14

THE COMMISSIONER: Yes.

15

16

17

18

19

20

21

22

23

MR. HUNT: Q. About half way through the notes you see propranolol was administered, and that after its administration the baby remained markedly cyanosed and extremities cool and respiration laboured, so that another dose was administered at approximately 3:55; Dr. Jedeikin being called before that last dose. Then the baby, the apex began to dip, it was approximately 72 and I think this is perhaps what you are referring to, the atropine was given at this point with good effect and then morphine.

24

25

Now it would appear that at least the



DD4

1

2

3

4

5

6

7

8

9

10

11

12

13

14

15

16

17

18

19

20

21

22

23

24

25

propranolol that was administered on the first occasion didn't produce the expected result inasmuch as the baby remained cyanosed and then more was given.

A. Yes.

Q. I guess what I am suggesting from my reading of it you say it wasn't an inexorable decline at this point, but it certainly would appear that there wasn't much in a positive way that happened to the baby once the situation became to develop at 3:45?

A. Well, I don't know, you would have to ask Miss Nelles I guess what she meant by "Atropine was given at this point with good effect". That is certainly 10 minutes after the start of events at 3:45. I am not suggesting, it sounds reading this, you know, there is always difficulty interpreting what other people mean, but it sounds like this was a rather precipitous event at 3:45. I guess it might be compatible with intravenous administration 15 minutes before of digoxin. Then why is it written that the baby was resting comfortably until about 3:45?

Q. We don't know.

A. The scenario you are painting just seems very unlikely to me.



DD5

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25

Q. We will have to I suppose look at the question of what happened before 3:45 at some other point; but in terms of what we see here as the baby's distress beginning at 3:45, are you satisfied that that is as consistent with the beginning of the effects of digoxin taking place as with anything else that we have heard?

A. Well, no. I think I have told you repeatedly that that is more consistent with the natural cause of this child's heart disease, and that it is likely whatever sequence of events is attributable to digoxin begin some time after that. The manifestations of digoxin toxicity are so vague, that almost anything can happen. So I can't say it is incompatible at all. You know, I surely don't want to be that dogmatic. I think if you move back much before 3:45 you are then going to have to postulate multiple vials, and that is possible too.

Q. Well if the baby was in her room at 3:44 or 3:43 by itself and someone came in and administered an IV dose, I take it that what we have here beginning at 3:45 is not incompatible with that?

A. No, it is not incompatible.

Q. Nor is it incompatible with



DD6

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25

the evidence you have given with respect to that size of a dose that is one adult vial producing the results that we see at 4:30 in the blood and in the tissue after death.

A. You are making a rather major assumption, you are saying the effect of that one adult vial 3 or 4 minutes.

Q. I don't want to assume it but you see we have heard ---

A. But that is the assumption you are making I am just stating it.

Q. But we have heard evidence to the effect that it can act very quickly, it can take longer to act. It seems to me there is a certain number of variables here that depend on the baby and the baby's condition. I don't want to make an unreasonable assumption.

A. No, but I mean your assumption here would be more attributable to propylene glycol perhaps than attributing it to digoxin. Actually reading Miss Nelles' notes she is really talking about the onset of generalized rigidity and a kind of seizure activity, and perhaps that is more compatible with propylene glycol although it is not strictly speaking characteristic either.



1

2

3

4

5

6

7

8

9

10

11

12

13

14

15

16

17

18

19

20

21

22

23

24

25

DD7

Q. Perhaps in fairness to you I will just advise you as to what Dr. Spielberg said with respect to that, and it perhaps amounts to no more than quibbling. In dealing with this same issue, in Volume 57 at page 2603 he said, at line 7 in answer to a question:

"Q. All right. So, as far as you can take it without getting into guesswork, we are dealing with that period 3:45 to 4:20 or shortly before and not moving back from that to any appreciable extent, is that correct?

A. In a general sense I think that would provide the most reasonable pharmacological explanations, albeit that one could produce a model that could go back further."

Now do you have any serious disagreement with that he has said there?

A. No, not really.

Q. And I take it the reason, or one of the reasons why we have selected an adult ampule has to do, for this particular calculation, has to do with the fact that that is, once you move beyond that you are into multiple vials and that



1

2

3

4

5

6

7

8

9

10

11

12

13

14

15

16

17

18

19

20

21

22

23

24

25

suggests more complications to the calculations that you have to make with respect to the digoxin in the tissues and the time at which it was given?

A. Yes, I guess, it is just commonsense.

THE COMMISSIONER: Do you agree?
I would have thought it had something to do with the delivery of it, isn't that it? The reason you suggest one vial is, whether by accident or design, the delivery of more than one vial becomes a very complicated transaction, does it not?

THE WITNESS: Not necessarily. I mean, you can pre-suppose these things have to be drawn up into a syringe and once it is in the syringe it doesn't make a vast amount of difference. I think the one vial question is most germane to the question of whether or not there is a possibility of medication error. I mean certainly it is impossible to imagine somebody opening 10 ampules of pediatric strength digoxin, drawing them up into a syringe and giving them in error. Although I have seen people give 10 digoxin tablets to a patient because they read 2.5 instead of .25 milligrams. I have a little more trouble with the ampule question, I really don't think that that kind of error occurs, at least I



DD9 1
2 hope not in the Hospital for Sick Children. I think
3 if somebody were administering the drug intentionally
4 clearly they wouldn't want to open 10 ampules.

5 Q. That was my next question. I
6 mean, once we leave the question of medication error
7 aside and then we are dealing with the spectre of
8 an unbalanced person, or somebody, for whatever
9 reason is administering it, we really are then into
10 a certain amount of guesswork as to how they go about
it, aren't we?

11 A. Certainly.

12 Q. There would be nothing to stop
13 someone from going into a washroom and loading a
14 syringe in the privacy of that type of room or some-
15 where else and then going in with it already loaded?

16 A. No, of course I would imagine
17 that is what happened if there was an intentional
overdose.

18 Q. So there is no magic I suppose
19 beyond the one vial amount that we are using in this
20 calculation other than with respect to the accidental
21 drug error theory?

22 A. I think there are many other
23 logical reasons for imagining it is one. I mean,
24 in fact we are not really talking about 10 pediatric
25



1
2
3 vials, we might be talking about 20 or 30, or even
4 40. In some of these cases if you get back, unless
5 you postulate administration too close to the time of
6 death, then I would suggest to you that for 40 vials
7 of pediatric strength digoxin to disappear from a
8 ward this would be noticed even given the relatively
9 inadequate drug distribution system that we had in
10 1981.

11 Q. So I guess what you are saying
12 is we seem to be zeroing in on a number of vials which
13 would perhaps be the most compatible with somebody
14 either intentionally wanting to do this without being
15 detected, or would also fit with the possibility of
16 a drug administration error.

17 A. Yes, I guess that is correct.

18 Q. Once we move beyond that
19 drug administration error then we are no longer
20 confined to the single vial theory.

21 A. We are not confined to it in
22 any case I don't think.

23 Q. Except you say it makes it much
24 more difficult to conceive of any error when you are
25 opening more than one vial?

A. Oh, yes. If you open 40 ampules
of digoxin, there is a tremendous amount of garbage



DD11

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25

from that, you know, you have little bits of glass all over the place. It would be very difficult, and it would take you half an hour to draw up 40 ampules probably, by the time you snapped each one open and went from vial to vial, it would be a major undertaking.

Q. It is not the sort of thing one wants to do in any event in circumstances where they were doing something that they didn't want to be seen doing.

A. I certainly agree with that.

Q. Now, you were asked by Mr. Lamek this morning with respect to the effect on your opinion of accepting the facts of intentional overdose, with respect to Justin Cook. You indicated once you accept that insofar as Justin Cook is concerned then you would have to reconsider Miller, Baby Miller, in light of the timing of her death, and Justin Cook.

A. Not so much a question of reconsidering it, but I think you have to be influenced by the opinion on Cook.

Q. My point here is that insofar as the scientific analysis assists us here, really you have all of the factors now that can be plugged



1

2

into the equations to come up with the various
opinions, is that right?

3

4

A. We know all the factors we will
ever know, and I guess what I have been saying for
the last day and a half is we don't know enough.

5

6

7

Q. That is short of somebody
giving us more information?

8

9

A. The only information that will
help us to know the precise dose and when it was
administered and I don't think anybody is going to
tell you that.

10

11

12

THE COMMISSIONER: Or one of those.

13

14

THE WITNESS: Or one of them, that
is correct.

15

16

17

18

19

20

21

22

23

24

25



EE
DPcr

1

2

3

4

5

6

7

8

9

10

11

12

13

14

15

16

17

18

19

20

21

22

23

24

25

Q. So once we ---

THE COMMISSIONER: There must be a minimum quantity, assuming for the moment that digoxin caused the death, there must be a minimum quantity that would cause death and I suppose there must be a minimum level of digoxin?

THE WITNESS: Certainly there is. Unfortunately, we cannot know it with any certainty for any of these particular babies because they all had underlying heart disease.

THE COMMISSIONER: I agree, but there must be a level at any rate beyond - for instance, it is most unlikely that a paediatric vial delivered, even out of time or anything else, is likely to cause the death of any child, I would think; not knowing anything about it, but I would think it is not probable.

THE WITNESS: Generally speaking, that is right, unless you were talking about a very small child.

THE COMMISSIONER: With already a doubtful level?

THE WITNESS: With already a doubtful level and perhaps predisposed, as Cook was, to



1

2

digoxin.

3

4

THE COMMISSIONER: Assuming Cook had
no level at all, a paediatric vial would ---

5

6

THE WITNESS: I would not expect
that to be fatal, even for him.

7

8

THE COMMISSIONER: Would you expect
anything less than an adult vial to be fatal?

9

10

11

12

THE WITNESS: Probably for Cook,
yes, because of the predisposition to digitalis,
the fact that this type of structural heart disease
is made worse by digoxin, so he might have had a
fatal reaction to something less than an adult vial,
sir.

13

14

15

16

17

MR. HUNT: Q. The point that I am
getting at here, and I am not making it very clear,
I am afraid, in terms of scientific analysis, without
further information, you have given us all the help
you can give us.

18

19

20

21

A. I think that is correct.
I think the only scientific contribution to this is
to point out to you that there is a wider range of
possibilities than was probably credited in the
beginning.

22

23

24

25

Q. Fair enough. If it becomes
established that Justin Cook was murdered by an



1

2

overdose, that fact alone, the establishing of that,
does not add anything to the scientific analysis of
the case in respect to the other babies?

3

4

A. Not at all.

5

6

Q. When you say you then have

7

to consider Miller in the same category, it was
because of the timing?

8

9

A. Absolutely. Purely a
question of logic, nothing to do with science.

10

11

Q. Once we establish, if it

12

is in fact established that Cook was in fact
murdered then the factors that we look to to assist
us with respect to the other children are really non-
medical factors?

13

14

A. I think that is correct.

15

16

Q. They are pieces of

17

information that may have nothing to do with the
drugs themselves, but have a lot to do with circum-
stances?

18

19

A. I think you will still have

20

a range in each individual case from very
equivocal evidence to less equivocal evidence and
you will have to be influenced by that. It is not

21

22

fair to say that the scientific data is completely

23

irrelevant. In many cases it is purely qualitative

24

25



1

2

so then it is extremely equivocal.

3

4

Q. But the additional
information we will have to add to that will be
essentially non-medical information?

5

6

A. I agree with you.

7

8

MR. HUNT: Thank you. Those are
all the questions I have.

9

10

THE COMMISSIONER: Thank you, Mr.
Hunt. Mr. Young?

11

12

13

14

15

16

17

18

19

MR. YOUNG: Mr. Commissioner, I
must ask your indulgence in this instance. Because
of our preparation for argument this afternoon and
meetings over lunch trying to inform Mr. Percival
of what will go on this afternoon, I have not really
had an opportunity of reviewing the Doctor's
evidence, and I have not been here throughout all
the Doctor's evidence. I wonder if I might ask
to be put somewhere down the line today and go on
a little later.

20

21

THE COMMISSIONER: I think that is
a desirable spot. I will just try it out for size.

22

23

Miss Kitley, are you prepared to
proceed?

24

25

MISS KITLEY: Mr. Knazan is going
to go next, sir.



1
2 THE COMMISSIONER: All right. You
3 are the good Samaritan around here, All right, you
4 proceed.

5 MR. KNAZAN: I am in about the
6 same position, but I was here for the evidence so
7 I will - I think everyone will benefit because I
8 will be brief, as I am not prepared.

5
8 CROSS-EXAMINATION BY MR. KNAZAN:

9 Q. Doctor, I represent Mrs.
10 Christie who is a Registered Nursing Assistant on
11 4A.

12 With respect to Baby Pacsai, just
13 picking up from Miss Forster, besides the notes in
14 the chart about the return to normal rhythm, Dr.
15 Costigan also testified that the baby was stable
16 except for the electrolyte readings. He said he
17 had three stable hours in ICU from the time he took
him up until the time of arrest.

18 Would that assist you in answering
19 Miss Forster's question?

20 A. I don't think it would
21 change my response particularly. Perhaps it makes
22 some scenario like I drew here a little more likely,
23 that you have repetitive smaller doses, but it
24 is not completely unheard of by any means for
25



6 1
2 people with toxic concentrations of digitalis to
3 have periods of normalcy.

4 Q. Does it change the weighting
5 of your probabilities as between a dose on ICU
6 bringing on the final events at arrest or a dose
7 previous to 5:30 causing both incidents?

8 A. It is very difficult. It
9 really puts you in a position of almost - if you
10 believe a dose of any kind has been given it really
11 puts you in the position of having to believe there
12 were two doses, as indicated here.

13 The alternative to that is believing
14 that the initial level at 6 o'clock is due to this
15 pathophysiological perturbation, high potassium
16 leading to release of dig. leading to high serum
17 digoxin measurement, and that is possible, and maybe
18 that is all that ever happened. Maybe there was
19 not another dose at all. Maybe we then just saw
20 the natural progression of the disease. The third
21 alternative is that that happened initially and
22 then a further dose - an initial dose, in fact, was
23 given in the ICU.

24 Q. Now, whichever one of the
25 now three alternatives it is, do I still under-
stand that you favour the theory of oral dose with



1
2 regard to this baby.

3 A. I would still favour an
4 oral dose theory. I think if an intravenous dose
5 was given, it was certainly not of an order of
6 magnitude very far removed from normal oral dosage
7 or a small oral dose.

8 Q. I think Mr. Lamek asked you
9 if it was possible to give an oral dose in an ICU
10 vial?

11 A. Yes.

12 Q. You said yes.

13 A. Yes.

14 Q. By that you contemplate
15 drawing up the dose in the syringe and squirting
16 it into the mouth, or breaking off the top of the
17 vial and pouring it into the mouth. What did you
18 mean by that?

19 A. Usually that sort of
20 medication would be administered through a syringe
21 or medication spoon or something like that. There
22 are many ways it could be given. Probably by a
23 syringe in ICU.

24 Q. You said it would take
25 about half an hour to open 40 so I assume this
procedure would take about 40 seconds or 45 seconds?



8

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25

A. To open an ampule?

Q. If there was only one, yes.

A. Oh yes, seconds.

Q. And seconds to squirt it
into the mouth?

A. Yes.

Q. What is the alternative
way of giving an oral dose, through a bottle?

A. There might be a tube
feeding running, for example. I don't think there
was in this case.

Q. So by oral you are including
the nasal gastric tubes?

A. I am sorry, when you say
alternative means?

Q. Alternative ways of giving
an oral dose. I am trying to establish what that
means. One way is drawing it up in the syringe
and squirting it into the mouth. What are the other -
I assume there are others?

A. There is oral digoxin
solution available.

Q. How would that be administered?

A. Well, the same fashion,
usually with a dropper, perhaps. It depends on the



1
2 dose you are administering. If you are planning to
3 administer 2 or 3 mls of the paediatric elixir
4 you would probably do it through a syringe. If
5 you were measuring normal therapeutic doses you would
6 probably do it with a dropper.

7 Q. I do not want to take you
8 out of your area but I notice you did say, because
9 of your position, you know a lot about the pharmacy
10 in the Hospital as well as pharmacology?

11 A. I said I know something.

12 Q. Yes.

13 A. It is not given to man to
14 know much about the operations of pharmacies.

15 Q. Is it correct, though,
16 that any of the oral doses you just described might
17 be likely to attract attention. That is, as
18 opposed to putting it into the IV, those three
19 things which you just described seem to be out
20 of the ordinary in the treatment of the baby?

21 A. No not at all, unless the
22 baby was not on any oral medications. I don't
23 think any nurse or physician would look twice at
24 the sight of somebody administering a dropper full
25 of medication to a baby. It might be a little bit
unusual when a baby had just arrived in the Intensive



1
2 Care Unit and there were probably several people
3 around and involved, people who were familiar with
4 the medications being given, they might be surprised.

10 Q. With your knowledge that
5 you have of the pharmacy, are you aware of which
6 staff people are entitled to administer which drugs
7 in which ways. Do you have first hand knowledge of
8 that, that is, doctors as opposed to nurses as
9 opposed to RNA's.

10 A. I am as aware of it as
11 anyone I guess but it is a very troublesome issue
12 in a hospital like ours which is very much a tertiary
13 care hospital and has a lot of complex and specialized
14 units. On some wards nurses would be allowed to
15 give certain drugs that they would not normally give
16 on other wards. It is very difficult to write
17 down specific lists and actually we are still in
18 the process of doing this. There are policies in
19 force in virtually every ward that have been
20 derived by the head nurse, usually in consultation
21 with the physician who is responsible for the ward
22 and usually approved by the Department of Nursing.

23 To suggest to you that there was
24 any uniform policy in place at Sick Children's
25 in 1981 or November 1983 would be misleading, I



1

2

think.

3

4

5

6

7

8

9

10

11

12

13

14

15

16

17

18

19

20

21

22

23

24

25

Q. There has been one thing alluded to and it may be proved, so if you do not know just tell me. Were you aware that Registered Nursing Assistants were not allowed to give any medication at the time in question?

A. I believe that is a legal dictate from the Hospital Act. I'm aware of this. They are allowed to give medications of certain kinds in nursing homes but in a general hospital, if they give them at all it would be under the direct supervision of an RN, I would imagine.

Q. I wonder if one of my friends could lend me Exhibit 48. I was not expecting to cross-examine, so I came without it.

Am I right that you assisted Dr. Spielberg in writing the appendix referring to the ---

A. Appendix 2, yes.

Q. I will go at it another way. You testified to Mr. Lamek that as far as the last three babies he mentioned, Lombardo, Belanger and Hines you were prepared to accept that they had definitely received digoxin?

A. I said provided that we take as gospel the reported analytical results.



1

2

Q. Yes.

3

A. I certainly have not seen

4

them and to my knowledge nobody at the Hospital

5

has seen them but if we accept that, particularly

6

the gas chromatography results on Lombardo and

7

Belanger, then I would be prepared to say they had
received digoxin.

8

Q. And this is despite all your

9

concerns about loss due to desiccation and fungus

10

and ---

11

A. I do not think one can

12

attach any significance whatsoever to the absolute

13

measurement. I think you can take it as qualitative,

14

if you find digoxin positively and it is positively

15

identified as being digoxin and not some other

16

chemical of similar structure then it really

17

doesn't matter what the concentration is. You

18

Q. Dr. Bain, and I am flipping

19

through as I ask you questions, with respect to

20

that put something in his report and gave some

21

evidence that he thought, depending on what the

22

pharmacologists said, and now you are here, that

23

with either substance X or whatever it is which

24

gives a low reading, either under .5 or .2 the

25



MacLeod, cr.cx.
(Knazan)

1
2 effect of, first, a post mortem to pre mortem
3 multiplier and this unknown factor for burial
4 for a year could give a reading that high, even
5 though there was no digoxin in the body. I just
6 want to establish that you disagree with that?

13 THE COMMISSIONER: That is not my
7 understanding. I would not disagree with that
8 at all, but what he says is if it is digoxin
9 it follows that digoxin was administered. I think
10 that sounds like a pretty logical proposition to
11 me.

12
13
14 - - - -
15
16
17
18
19
20
21
22
23
24
25



F/BM/ak

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25

THE WITNESS: I hope so. But I am qualifying my reply to say that provided that the specificity of the analytical technique is adequate and as far as I understand it for Belanger and Lombardo it is adequate, although, we haven't seen that data. If we don't see it somebody should certainly see it, preferably somebody with good analytical credentials. But if they agreed that that really is digoxin and not some other similar substance then I think Dr. Bain's comments notwithstanding, it is pretty good qualitative evidence that the digoxin was given.

THE COMMISSIONER: You see, if it isn't substance X, substance X couldn't have anything to do with it.

MR. KNAZAN: Q. Okay, I think that covers the substance X but as far as a no digoxin reading being worked up to that level.

A. Yes.

Q. Are you saying you are satisfied, still satisfied that whatever those multipliers are that these babies were given digoxin?

A. As long as you like and you don't get any more than zero.

Q. Yes.



1

2

A. Provided you have got something

3

there that you can positively identify as digoxin,

4

whether it is one molecule or 10 million molecules,

5

it doesn't matter at all. I think as soon as you

6

prove unequivocally that there is one molecule there

7

then you can say that they received at least one

8

dose of digoxin of some magnitude. It is not getting

9

very far, but since they weren't supposed to receive

10

any...

Q. Now, on the Saturday night,

11

March 21st, you were involved by telephone about the

12

orders to get the digoxin off the ward, is that right?

13

A. Yes, my discussions at that time

14

were all on the phone.

15

Q. But you knew about Miller and

16

you knew about Pacsai from the previous week. Was

17

it the feeling then that this had to be done intra-

venously?

18

A. Oh, I don't think we got to

19

the point of discussing the route of the administra-

20

tion on Saturday night to be honest. I knew nothing

21

more than the absolute values. So, I'm sure I had

22

no opinion whatsoever on the route of administration.

Q. And you don't remember any of

23

the others who you talked to on the telephone

24

25

FF2



1

2

3

4

5

6

7

8

9

10

11

12

13

14

15

16

17

18

19

20

21

22

23

24

25

THE COMMISSIONER: Yes, thank you, Mr. Knazan. It is 3:30 now and we are going to have this meeting. I don't know whether the necessary participants are here. Is Mr. Percival here?

MR. YOUNG: I'm not sure if the combattants are here or not yet, Mr. Commissioner. I will check and let you know if you like.

MS. KITELY: Mr. Commissioner, speaking of combattants, I wonder if I might make a comment on the constitution of this meeting. I gather that Messrs. Sopinka and Percival are to attend and I am assuming Miss Forster as Mr. Strathy is absent. I'm not quite clear on the purpose of having ---

THE COMMISSIONER: Well, I am not making any decision. It is merely a sort of a pre-trial motion to see if it can be resolved and if it can be resolved then it is resolved so far as they are concerned, if it is not resolved so far as you're concerned you are free at any time to take any kind of position you like.

MS. KITELY: Is there any reason, sir, why other counsel might not be invited to this meeting?

THE COMMISSIONER: Space is one of



F5
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25

them.

MS. KITELY: Assuming space.

THE COMMISSIONER: I was thinking
of having it in this room.

MS. KITELY: Assuming space could
be overcome, sir.

THE COMMISSIONER: Well, what interest
do you have in the police report outside of idle
curiosity? I can understand that, I think there is
nothing like reading something you are not supposed
to read, but is there any other purpose that it
would serve you?

MS. KITELY: I have an interest
other than idle curiosity.

THE COMMISSIONER: I know, I'm joking,
but what is that interest?

MS. KITELY: The position that we
will be taking is to oppose its distribution, sir,
and if there is a remote possibility that a decision
of part of such decision will be made without having
it heard in Court ---

THE COMMISSIONER: Well, I'm not
going to make any decision this afternoon. What I'm
going to see is if perhaps there can be some compromise
reached - you are opposed to it, what, being



1
2 distributed to whom?

3 MS. KITELY: To all counsel.

4 THE COMMISSIONER: To all counsel?

5 MS. KITELY: Yes, sir. I am not
6 prepared to argue the issue at this point, I just
7 want to indicate that I have an interest in the
8 issue and would like to be present whenever it is
9 discussed.

10 THE COMMISSIONER: Well, I don't know
11 what to do about that, Miss Kitley. I suppose -
12 have you got an interest in it too?

13 MR. ROLAND: I think so, I think
14 the Hospital has an interest in it too.

15 THE COMMISSIONER: Well, I don't
16 think that either you or Miss Kitley have nearly the
17 interest that the counsel that I have asked to come
18 to this meeting have.

19 MR. ROLAND: Well, I don't know,
20 it is interesting you say that, Mr. Commissioner.
21 I don't know how you can come to that conclusion,
22 quite frankly, unless you have seen the report and
23 I haven't.

24 THE COMMISSIONER: Yes, I have, it
25 was delivered to me I think about two days after the
appointment.



FF7

1

2

3

4

5

6

7

8

9

10

11

12

13

14

15

16

17

18

19

20

21

22

23

24

25

MR. ROLAND: Well, if you have seen the report then, Mr. Commissioner, it seems to me that it is important that we all see it.

THE COMMISSIONER: Well, that's quite right. It is right, I can't help it though. This is something that happened. But also, if the report is privileged in some way I don't think even if it is privileged I'm not allowed to, under the terms of the Act, I'm not allowed to let you see it. If the report is filled with monstrous hearsays why should I give it distribution if it is not going to be used and no part of it is going to be used?

MR. ROLAND: Well, what concerns me is that you have read it - you have told us now, Mr. Commissioner, you have read it and if it contains no criticism whatsoever of my client or any of the people employed at the Hospital at any relevant time than I have no - I think I have no legitimate interest in it but if it contains any criticism of the Hospital ---

THE COMMISSIONER: Well, no, if it contains anything in there that is going to be offered by Mr. Lamek then of course it has to be - well, I say of course I haven't heard the argument on it but that portion of it has to be released.



FF8

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25

But, you see, I really hadn't intended. My action, believe it or not, is intended to be pretty innocent. I just want to sit down and knock a few heads together, that's all. That is all. I don't intend to make an order at the moment that will affect anybody and I am quite prepared to undertake that. Do you mind if I just see them for a while if I promise faithfully I won't do anything because otherwise we just have to argue the argument and we can't have it now and I have dragged these important people away from their important positions and God knows what is going to happen to litigation this afternoon because of that.

What really basically do you object to, what is your objection to my seeing them privately?

MR. ROLAND: At your urging, as you put it, I am not going to say that you can't see them. What I am concerned about is that you have told us just now you have read the report.

THE COMMISSIONER: Well, I would have told you long before if you had asked me. I didn't keep that from you, but the police sent it to me and I read it.

MR. ROLAND: Well, if it contains any criticism at all of the Hospital then I think it



FF3

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25

expressing the opinion to you?

A. No.

Q. Were you involved with Dr. Fowler in drawing up the order to get the digoxin off the ward?

A. I didn't speak to Dr. Fowler on the Saturday night, I spoke to Dr. Carver and I imagine it went from us to Dr. Fowler.

Q. But it would have been your feeling it would have been wise to get everything off, intravenous and oral?

A. Oh, yes. Certainly our intention was to lock it all up but as we found out there was a lot of digoxin in various places in the Hospital and in fairness I don't think there is any way that Dr. Costigan could have been expected to know where it was; I certainly wouldn't have known where it was. I think he would have had to have a major search as was required on Sunday in order to find it all. As I recall, the idea at the time was to try and do it without disturbing the Hospital too much since there was a certain amount of uncertainty about what was going on. So, I imagine he made his inventory with a certain amount of discretion.

MR. KNAZAN: Thank you, Doctor.



1
2 is important that you having that information, having
3 read it that we have it available to us.

4 THE COMMISSIONER: Well, if I am
5 going to use any part of it you are certainly going
6 to receive it, there is no question about that. I
7 don't intend to get - I know that it may be I am
8 legally entitled to but I don't intend to get any
9 information and make use of any information against
10 anyone without that person having all of it. At the
11 moment nothing that is in that report has been
12 presented in evidence. Some of it may be, I don't
13 know. I don't know what Mr. Lamek has in mind with
respect to it.

14 I will bear in mind what you have
15 to say, let me carry on with this secret of or
16 surreptitious or whatever word you want to call it for
17 just about 15 minutes and then we will come back.
All right, can we break off then? Yes?

18 MR. OLAH: I was just going to ask
19 that in case your surreptitious enterprise is successful
20 with respect to Mr. Sopinka then my respectful
21 submission it should apply to everyone on the Trayner
22 team.

23 THE COMMISSIONER: It may. That may
24 be right, that may be right, we will just have to
25



FF10

1

2

see how successful he is.

3

All right, let's adjourn for 15

4

minutes.

5

---Short recess.

6

7

8

9

10

11

12

13

14

15

16

17

18

19

20

21

22

23

24

25



DM.jc
GG

1

2

--- Upon resuming:

3

MR. TOBIAS: Mr. Commissioner, if I could just for the moment, I would like to file at this time my reply argument.

5

6

THE COMMISSIONER: Thank you very much.

7

8

MR. TOBIAS: To the written submission.

9

10

THE COMMISSIONER: If there are any other documents to be filed I will be happy to have them.

11

12

MS. KITELY: I would like to file our reply argument and copies have been made available to all counsel.

13

14

15

16

17

18

19

20

21

22

23

24

25

THE COMMISSIONER: Right, thank you. For the benefit of everyone, that private meeting did not result in any immediate conclusion. Mr. Percival is taking certain propositions that have been made to him to discuss with his client. He will let us know some time next week. We will not, even if he rejects all the proposals and we have to argue the question, we will not be doing it on Tuesday. The only matter we will be arguing on Tuesday after the judgments will be the question of notice and the motion brought by Mr. Olah. Now, any questions on that? All right.



GG.2

1

2

Now, Mr. Olah, I think you are next.

3

No, I am sorry, what about you Mr. Young?

4

MR. YOUNG: I prefer Mr. Olah, you know what I was doing during the break.

5

THE COMMISSIONER: Yes, all right.

6

CROSS-EXAMINATION BY MR. OLAH:

7

8

9

10

11

12

Q Doctor, my name is Olah and I act for Janet Brownless who is one of the Registered Nursing Assistants who is still on Ward 4A. Some of my questions hopefully will be a little different than the ones you have encountered, and I would like to first start off with the child, Kristin Inwood.

13

14

15

16

As I recall your evidence from yesterday, and throughout the discussion that we are going to have for the next couple of minutes, I would like you to assume the validity of the serum reading of 491 nanograms, all right?

17

A. Fine.

18

19

20

21

Q I think when you discussed that reading with Mr. Lamek yesterday you indicated that given the nature of the reading you did not believe that that indicated a steady state concentration?

22

23

24

25

A. I think it is almost impossible to conceive of that being a steady state concentration.

Q In fact I think you indicated



GG.3

1

2

that administration, assuming a valid reading,

3

occurred at the top of the alpha phase?

4

A. That is correct.

5

6

Q. Now, I think somewhere along the way you mentioned that the range of multipliers you have experienced are anywhere from 2 to 4, is it?

7

8

9

10

11

12

A. Well, the average on data in our Hospital is 3.8 in fact. The range taking all the values that we know of from the literature and various places including the Gary Murphy baby, is as high as, well, I think Murphy is 14 or 15 actually if you calculate it out, so the range is say 2 to 15.

13

THE COMMISSIONER: Excuse me just a minute, gentlemen. Thank you, I am sorry.

14

15

16

17

18

19

20

MR. OLAH: Q. Now normally though, other than for unique situations like Murphy, which is probably explicable by the very unique situation involved there, would a multiplier of 4 be a reasonable one to use in a case of this kind? Because I think at one point you even said in readings of this kind you would look to lower readings say 25 per cent?

21

22

A. Lower multipliers?

23

Q. Yes.

24

A. Yes, that is true.

25



GG.4

1

2

3

4

5

6

7

8

9

10

11

12

13

14

15

16

17

18

19

20

21

22

23

24

25

Q. Let us just for the sake of being conservative use a multiplier in this case of 4 and let's work with an ante mortem level of about 125 nanograms.

A. All right.

Q. Bearing in mind that it was 491. Would that indicate to you, Doctor, that we can rule out oral mode administration in this case, given the very large quantities that would be required to reach that kind of a level?

A. It is very difficult for me to imagine getting up to that level following oral administration without death occurring prior to that degree of absorption being completed.

Q. All right, we can't rule it out with certainty as you pointed out throughout your evidence in the past two days. Can we say with a fairly high degree of certitude that oral mode of administration is not probable in this case?

A. I think you can.

Q. Now you will recall that in this case, Doctor, the arrest occurred at 2:30 a.m. and death was at 3 o'clock in the morning.

A. Yes.

Q. Assuming consequently some sort



GG.5

1

2

3

4

5

6

7

8

9

10

11

12

13

14

15

16

17

18

19

20

21

22

23

24

25

of an IV administration; let's use first the single vial concept or hypothesis. What I would like to know from you, Doctor, is what is the maximum time that you feel one can go back for the administration of one vial of digoxin? What is the maximum period of time back from death that that could have occurred?

A. Taking the minimum as being a few seconds; do you want to go in the other direction now?

Q. I am not interested in the minimum.

A. It would help me to see the chart, is that possible?

THE COMMISSIONER: Yes, certainly, this is the Inwood chart.

MR. OLAH: Exhibit 113.

THE COMMISSIONER: Unfortunately I sent the Registrar away.

THE WITNESS: Does anyone have a copy that I can look at?

MR. LABOW: He can have my copy.

THE WITNESS: Can you help me with the page number?

MR. OLAH: Q. What particular document are you looking for?



GG.6

1

2

A. The description of the arrest.

3

Q. Yes, the terminal events you

4

will find are to be located at page 62 and 63, Doctor.

5

On page 63 you will see the notes of Nurse Harwood

6

Jones commencing at 2 o'clock.

7

A. I am sorry, which notes are

those?

8

Q. Page 63, they are the progress

9

notes of --

10

A. Start 0200.

11

Q. 0200.

12

A. "Babe was feeding poorly all

13

night .. fed by D tube; breast

14

milk ... ",

is that the one?

15

Q. That is the one.

16

A. Yes.

17

Q. You see at 0200:

18

"Monitor strip showed abnormalities.

19

TL notified. Resident called."

20

A. Yes, I am reading that. Going

back on the page before.

21

Q. You will see the note of

22

Dr. Mounstephen.

23

A. That is right, I am looking at

24

25



GG.7

1

2

the ones that says "25 called".

3

Q. That is the one.

4

A. "Child with known AS; bradycardia;

5

IV adrenaline and so forth ... "

6

I mean, he is describing the resuscitation procedure
and he says:

7

8

"No electrical response; no response
to CPR; resuscitation stopped

9

approximately 30 minutes after

(2)

10

starting."

11

I may be wrong, you would have to ask Dr. Mounstephen,

12

but that implies to me that there was virtually no

13

circulation during this period of resuscitation, that

14

it was generally a futile attempt and that circulation

15

did not occur to any significant degree during that

16

time, although I guess it has to be said the

17

cardiopulmonary resuscitation is properly carried

18

out. I think we said this yesterday, that there must

19

be some circulation. But the import of that is that

20

there may have been very little distribution occurring

21

within that period from the time of administration of
a dose of digoxin until the time when the resuscitation

22

was stopped.

23

So I think you can - the admini-

24

stration - we may be able to go back some period -

25



GG.8

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25

I'm sorry, I don't think we can go back, we still can't go back very far before 0200, that is the question you are asking me?

Q. Not really. What I want to know is the maximum time that in your belief, given the one vial hypothesis, one can go back the maximum time for administration. You see, because my client was off early in the evening.

A. Yes.

Q. Well, I am trying to establish obviously she could not have been there, Doctor.

A. I understand. I don't think one could go back really more than minutes, seconds even before 0200.

Q. Fair enough. Now let's then talk about a multiple vial theory. Bearing in mind the kind of terminal events you see in that situation, let us assume a fairly large loading dose of multiple vials. What is the maximum time that in your opinion that kind of a dosage could be given? Now, I know you may have problems by saying, how many vials. Let me ask you to hypothesize some sort of a realistic scenario with respect to a multiple dosage loading, and using that kind of a load I would like you to tell us what is the maximum outside time for its



GG.9

1

2

administration to result in that kind of a terminal event?

3

4

5

6

7

8

A. Well, it's a very - again I don't think we can go back very far, mainly because that level is so high. So we are talking about - I mean if we are talking multiple vials as an explanation we are probably talking about - really a very large dose of digoxin.

9

10

11

Q. What do you mean by that?

A. Well, do you want me to be

specific, how many milligrams, would that be it?

12

Q. Roughly.

13

14

15

16

17

18

19

20

21

A. I think as I explained to you yesterday. I mean, if you take death occurring at the moment of administration these numbers that are on the blackboard here are still valid. If we are talking about 49 micrograms as being enough to account for that concentration, if no distribution occurred whatsoever. So we are saying one paediatric ampule could have done it, assuming that it is given quickly death ensues, there is no circulation, no distribution, that is obviously an extreme hypothesis.

22

23

24

25

Say we go back to ten times the dose and say giving one adult ampule, but with very little distribution occurring afterwards, we are still - we



GG.10

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25

still are left, you would have to be left with the
conclusion that death would occur very, very rapidly.

Q. All right. Again I would like
to return to the question I posed, what would be the
outside maximum limit for administration in the
multiple dose situation?

A. Okay. Multiple or higher, one
adult ampule?

Q. We have already covered the one
adult ampule situation, I am looking at the maximum
probable or possible loading dose and what kind of
a time parameter, maximum time parameter we can be
looking at.

-

-



H/DP/ko

1

2

3

4

5

6

7

8

9

10

11

12

13

14

15

16

17

18

19

20

21

22

23

24

25

A. Well, if you get into that type of scenario you are talking 10 minutes before 0200 at the outside. If I follow you correctly, you are talking about giving sufficient amount of digoxin that peak concentration might have been 2,000 nanograms per ml. We have already got an unbelievably high concentration at 491. Even if we knock that down to one-quarter, say it is 125, it is still an unbelievably high concentration.

If we move it back --

THE COMMISSIONER: Any thoughts on what the highest concentration a child could endure at any point? The top of the alpha curve, before there has been any - I suppose the child will not die until there has been the slightest distribution. But there could be at the top of the alpha curve a little distribution.

THE WITNESS: Yes, that is correct, unless death was due to propylene glycol as has been suggested, in which case we do not really have to pre-suppose any distribution of digoxin but logically, if we attribute the death to digoxin we have to allow some time for distribution.

THE COMMISSIONER: There is a certain dosage I suppose that would be so instantaneous, the



HH 2

1

2

3

4

5

6

7

8

9

10

11

12

13

14

15

16

17

18

19

20

21

22

23

24

25

distribution would be right almost at the moment of administration, because the very first administration would kill the child.

THE WITNESS: If it is a huge dose, is that what you mean?

THE COMMISSIONER: Yes.

THE WITNESS: Yes, I would agree with that. So we are really talking potentially about a huge dose.

Perhaps I should answer your question first. There is certainly a report of suicidal overdose of an adult taking a 90 25 milligram digoxin tablets and here you don't have the high peak, you have the absorption, but achieving a steady state concentration of 200 nanograms per ml without the patient dying, but that is an adult with a normal heart.

Any figure that one would give for children would be arbitrary. There is one case report of a child surviving an apparent steady state concentration of 30 nanograms per ml.

THE COMMISSIONER: What does that represent in the amounts that the child took?

THE WITNESS: The amount given? I could probably tell you the exact figure.



HH 3

1

2

3

4

5

6

7

8

9

10

11

12

13

14

15

16

17

18

19

20

21

22

23

24

25

THE COMMISSIONER: You will have to tell me in vials because I get lost when you start talking about micrograms.

THE WITNESS: I can find the exact amount that was taken in that case. Just give me a second. It is actually, that particular case, a 10 year old child, out of infancy, for sure, a 10 year child taking 16 milligrams of digoxin so that is 500 micrograms times - that is 32 adult - would be the equivalent of 32 adult ampules taken orally, and surviving. So again it is arbitrary but it is clear that some individuals can tolerate rather large amounts and rather high concentrations without dying, but we have gotten away from your question.

MR. OLAH: From my question - that is assuming a multiple loading situation and I want to know the very outside time parameter or time limit for its administration.

THE COMMISSIONER: I don't know whether he can answer, but surely you have to give - do you not have to give the multiple dose, what it is?

MR. OLAH: That is what we went through a moment before that, Mr. Commissioner. I had asked the Doctor to take a loading dose that he thought was appropriate, a multiple loading dose, and I think he



HH 4

1

2

gave me a figure, what was it, 10 vials?

3

THE WITNESS: Ten adult vials.

4

5

MR. OLAH: Q. Let us use 10 adult vials. What would be the maximum outside time parameter, somewhere around 2 o'clock again?

6

7

A. I think at the outside the child might survive 10 minutes after that kind of dose, a child of this age with this heart disease.

8

9

10

11

12

13

Q. So what you are saying in effect is if you are going for a multiple vial situation or from a single vial situation to a multiple vial situation then administration would have to occur closer to death, not further back than the single vial administration?

14

15

A. Yes, I think that is correct.

16

17

18

19

Q. So in all cases when I am going to question you in this area so long as we establish the maximum outside time parameter for a single vial situation that is the maximum time period for administration. We are talking IV now?

20

21

22

23

24

25

A. Yes, for one vial.

Q. So if my client were off, and we will have evidence to this effect, the evening previously at 7:45, and as I posit it to you, arrest was at 2:30 and death at 3 o'clock, it is very clear



1

2

3

4

5

6

7

8

9

10

11

12

13

14

15

16

17

18

19

20

21

22

23

24

25

beyond any realm of possibility that she could have had no involvement whatsoever with that kind of administration?

A. I would certainly agree with that.

Q. Thank you.

THE COMMISSIONER: I hate to create a row - no direct involvement?

MR. OLAH: No direct involvement - maybe I should plead now, Mr. Commissioner - release my client and myself.

Q. I would like to then just deal with the sample for a moment, sir. Did you ever make any enquiries as to the life or mode in which that particular Inwood sample was kept in Virology?

A. I did not make any enquiries myself. I have read reports that described how it was kept.

Q. You expressed some concerns, and you probably have not seen the evidence of Mr. Cimbura. It was his evidence that he tested a sample which was heated and heating did not seem to have any impact or change on the measurement of concentration. Does that allay some of the concerns you expressed yesterday to Mr. Lamek about that particular sample?



1

2

HH 6

3

4

5

A. In fairness I think I would have to see Mr. Cimbura's data to comment on it. There are a number of factors here, this sample also sat in the refrigerator for nine months, it was heated --

6

Q. We will come to that in a moment.

7

8

9

10

11

12

A. It started out with what in honesty is an unknown concentration of digoxin in it and certainly an unknown concentration in red blood cells. I don't know whether Mr. Cimbura would be able to duplicate those conditions. If he covered all the bases, then certainly, and I believe his data, that would allay my concerns about it.

13

14

15

16

17

Q. As we understand it, the sample started out as a blood sample taken from the inferior vena cava on autopsy. It was then sent down to Virology. Do you know what happens to that sample, how the blood turned into serum in Virology? What is done to it there?

18

19

A. I would imagine they centrifuge it.

20

21

22

Q. Would the centrifuging or the spinning down cause any kind of a change that would alter the digoxin reading in the serum?

23

24

25

A. Not under normal circumstances except for the fact that a good percentage of the



1

2

3

4

5

6

7

8

9

10

11

12

13

14

15

16

17

18

19

20

21

22

23

24

25

digoxin that is present in blood is in the red blood cells, so in sedimenting out those red blood cells you are in fact removing a good three-quarters of the digoxin in the whole blood sample.

Q. So that in effect the digoxin reading in a blood sample would have been substantially higher?

A. In a whole blood sample.

Q. As opposed to serum?

A. That is correct. That does depend on the time after death at which it was taken and how much hemolysis there was in those red blood cells, and that is something I just don't know.

Q. Is there anything else that occurs in Virology to the serum?

A. I have no idea what they actually did with it at that point.

Q. Do you have any information as to what kind of container it was kept in while it was refrigerated?

A. No, I do not know that.

Q. In the normal course of events would there be a stopper or something on the container?

A. In the normal course of events certainly. You cannot put anything in a freezer



HH 8

1

2

without having it sealed; otherwise it just disappears.

3

4

5

Q. So that you do not have the concern of evaporation operating in that kind of a situation?

6

7

8

A. Well, I am sorry - I just implied that was in a freezer. Actually I think I was told it was in a refrigerator so I should not suggest that there is major desiccation on that basis.

9

10

Q. You would not expect major desiccation?

11

A. No, I would not.

12

13

Q. So that would not impact on the sample itself?

14

A. It should not.

15

16

Q. It should not. Do you have any explanation as to why the sample would have been heated? Is there any reason for that?

17

18

19

20

A. No, you will have to put that question to the virologist. I do not even know precisely what test they were doing. I think they were probably doing a rubella antibody titre if I recall the case, but how they do that is not known to me.

21

22

23

24

25

Q. I would like to go now, then, to the Pacsai case and go through the timing problem with you, Doctor. Do I take it that it is your opinion that



HH 9

1

2

3

4

5

6

7

8

9

10

11

12

13

14

15

16

17

18

19

20

21

22

23

24

25

we can rule out an IV mode of administration impact
by assuming that there is digoxin administration in
that case?

A. No, I think from what I have
said you can rule out administration of a large dose
of digoxin in Pacsai and I have certainly said my
intuition tells me if a dose was administered it was
administered orally, but these figures in red that are
up here right now are a scenario that I suggested an
hour ago whereby smaller intravenous administrations
could have been possible.

- - - -



IT/BM/ak

1

2

3

4

5

6

7

8

9

10

11

12

13

14

15

16

17

18

19

20

21

22

23

24

25

Q. All right. Well, I would like to go through the same sort of time calculation we went through in the Kristin Inwood case. Let us assume oral administration to commence with. You will recall that the transfer to ICU occurred about 6 o'clock in the morning. I would like to know what is the maximum outside time limit in which you feel that an oral administration of digoxin could have occurred in that case?

A. It is insufficient to give a concentration. If we were to believe for the moment that the measurement of 10 nanograms per ml ---

Q. Well, it was greater than 10 at about 6:30 in the morning.

A. Greater than 10 but the evidence is that it is probably 10.4 or something.

Q. Something, yes.

A. 10.6. If we were to assume that that is valid and it is not in any way confounded by a high serum potassium?

Q. Yes.

A. Then the likelihood in that case is that represents a peak concentration following the dose since there is no reason to believe that it went higher in the ensuing two hours, although, it



II.2

1

2

3

4

5

6

7

8

9

10

11

12

13

14

15

16

17

18

19

20

21

22

23

24

25

might have gone a little bit higher. So, I would think at the outside that would mean that the administration would have had to have been made at about 0400 at the very earliest.

Q. All right. And then turning to a single vial scenario, what would be the outside maximum in that case?

A. I'm sorry, are we back to intravenous administration now?

Q. We are back to intravenous, yes.

A. That is a little trickier to say with any degree of precision because we simply don't have any idea what the absolute peak concentration was. Now, I believe the trouble with Pacsai started at 5:30.

Q. That is correct, Doctor.

A. Am I correct?

Q. Yes. Have you got the chart there?

A. Yes, I have the chart here.

Q. You will find the reference on page 63.

A. 63. All right, that is 5:30, okay.

Q. About half way down the page



II.3

1

2

3

4

5

6

7

8

9

10

11

12

13

14

15

16

17

18

19

20

21

22

23

24

25

you will see the time notation on the left hand margin.

A. Yes.

Q. Asked to see Kevin because of anxiety re - I am not sure what that first word is but it is bradycardia after that.

A. Yes. Well, I think you have to make a number of assumptions here to answer your question.

MR. LAMEK: Episodes.

MR. OLAH: Episodes.

THE WITNESS: I mean, if you assume - well, there are two possible assumptions: on the one hand you can assume that the clinical events at 0530 had nothing to do with digoxin, and I think I went through this this morning. If that is the case then the administration could occur at almost any time prior - well, let me qualify that. It could occur an hour or two hours beforehand or at the time, at 0530 at the time when the clinical condition deteriorated. If you assume that digoxin in fact was causing this and it was given intravenously, then I think you are back to at least 10 minutes prior to 0530, although, it is possible that again with a smaller dose of digoxin if you could move back quite



II.4

1

2

a bit earlier than that.

3

4

Q. Could you in any realistic
scenario move back beyond 4 o'clock in the morning?

5

A. Not really, not realistically.

6

7

8

9

10

11

Q. All right. So, if the evidence
were to demonstrate that my client was off the evening
prior at 8 o'clock, again, would you conclude with me
as in the Inwood case that there is no possibility
that she could have been directly involved in the
administration of digoxin with respect to Kevin
Pacsai?

12

A. Yes, I would agree with that.

13

14

15

16

17

18

19

20

21

22

Q. Now, I'm sorry that I am going
to take a few minutes and I wanted to go through the
Pacsai situation because I was somewhat confused and
I wanted to clarify a couple of matters. I think one
of your major conclusions with respect to Kevin
Pacsai was that as between - as for the explanation
of elevated potassium if we were to choose between
digoxin or elevated potassium explaining that reading,
75 per cent confidence, your confidence level would
be that it is the digoxin that explains that elevation.
Do I have that correct?

23

A. Yes, that's what I said.

24

25

Q. And the three possible scenarios



II.5

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25

or causal factors that you posited with respect to the child's death, number one, was some sort of a cardiac conduction problem?

A. Yes.

Q. Number two was some sort of a pathophysiologic occurrence?

A. Yes.

Q. And thirdly digoxin toxicity?

A. Yes. And I think I added a fourth, a combination of the first two - first three, really.

Q. Now, you told us you are not a cardiologist or a pediatrician.

A. Yes, that is correct.

Q. And you were very helpful in that and very candid about it. I take it that you would bow to the opinions expressed to this Commission by Dr. Rowe and Dr. Bain with respect to the cause of death of Kevin Pacsai.

A. What are their opinions?

Q. Well, I will come to that.

A. Before I accept their opinions I think you ought to tell me what they are.

Q. Well, would you agree with me that they are probably more qualified in assessing



II.6

1

2

3

cause of death certainly with respect to cardiac problems than you would be?

4

5

A. Certainly, yes, in the case of Dr. Rowe, certainly.

6

7

8

9

10

Q. Not in the case of Dr. Bain?

A. Well, Dr. Bain is a general pediatrician. My speciality is general internal medicine. Certainly Dr. Bain has more experience with, you know, children, congenital heart disease than I do.

11

12

13

Q. All right. Well, are you then --

A. I don't want to quibble over that. I will accept their opinions.

14

15

16

17

18

THE COMMISSIONER: Well, you don't have to do that, no matter how Mr. Olah bullies you. You are entitled to hear what they said because they may well have said something that is ridiculous. So that you shouldn't be placed in that position. I don't remember them saying anything ridiculous.

19

20

21

MR. OLAH: I wouldn't dare to bully you because the Commissioner would set me straight right away.

22

23

24

25

Q. Let me put their evidence to you. As I recall Dr. Rowe's evidence his evidence was that the most plausible account was for the death



II.7

1
2 of Kevin Pacsai was the one given by Dr. Bain, namely,
3 a functional disturbance of the adrenal gland. Were
4 you aware of that opinion, Doctor?

5 A. I have read that in Dr. Bain's
6 report.

7 Q. All right. Were you aware of
8 Dr. Rowe's evidence or opinion in that regard?

9 A. Of Dr. Rowe's evidence?

10 Q. Yes.

11 A. No, I wasn't.

12 Q. You wouldn't disagree with
13 Dr. Rowe on that point, would you?

14 A. I don't want to disagree very
15 strongly but in fairness Dr. Rowe's expertise on the
16 adrenal gland is probably less than my own.

17 Q. Well, the point I'm making
18 is ---

19 A. We are not talking cardiology,
20 we are talking adrenal glands and this is something
21 that is more in the realm of pharmacology and
22 pathophysiology and in that area my expertise is
23 certainly equal to the other two.

24 Q. Well, certainly implicitly
25 by that statement he has ruled out cardiac conduction
problems as the causation of death in Kevin Pacsai.



II.8

1

2

3

4

5

6

7

8

9

10

11

12

13

14

15

16

17

18

19

20

21

22

23

24

25

A. He appears to have but I think he has fallen into the old post hoc erga propter hoc fallacy, whether or not there is a disorder of the adrenal glands in Kevin Pacsai, there certainly is no evidence that that led directly to his death.

Q. All right. Well, we will deal with that.

A. I certainly would disagree with Dr. Bain and Dr. Rowe both on that question.

-

-

-

-



II-2
BB/cr

1

2

3

4

5

6

7

8

9

10

11

12

13

14

15

16

17

18

19

20

21

22

23

24

25

Q. All right. Well, we will deal with that in a moment but what I wanted to make sure was that you don't disagree with Dr. Rowe's assessment that cardiac conduction problem doesn't appear to have caused Pacsai's death?

A. No, I accept that statement and I understand that he is probably saying that because of this period that was brought up an hour ago of three hours of apparent stability and I imagine that is what has coloured his thinking on that.

Q. All right. So that we can rule out one of the scenarios that you posited as the causation in this case?

A. No, with respect, I don't think you can rule it out at all. I will stick with the possibilities that I stated to you. I think I certainly would be influenced by the fact that Dr. Rowe does not feel that the cardiac conduction disturbance was likely severe enough to cause death and there is no question his experience in that area is infinitely greater than mine and he is probably right.

Q. All right.

A. Nonetheless, it remains a



2-2

1

2

possibility.

3

Q. Well, shall we agree on this,

4

Doctor, maybe we can agree on this one point that it

5

is a remote possibility?

6

A. Relatively remote, yes.

7

Q. All right.

8

Mr. Commissioner, I see it is 4:30.

9

I know that there are several other counsel who
wish to cross-examine. I am in your hands, I am

10

prepared to proceed, I will be some time yet.

11

THE COMMISSIONER: Yes. Well, we

12

don't know when we are going to get Dr. MacLeod

13

back. What do you mean by some time?

14

MR. OLAH: I would expect to be

15

about another 10 or 15 minutes, sir.

16

THE COMMISSIONER: Well, I think we

17

should dispose of you so that at least if we do

18

bring him back you won't have to be here. I am not
being rude.

19

MR. OLAH: But by disposing of me

20

does that mean that I can now leave, sir?

21

THE COMMISSIONER: You can leave,

22

yes. No, I think if we can do that. I guess it

23

is impossible to do the rest of it but I think it

24

would be good at least to complete your examination

25



MacLeod, cr.ex.
(Olah)

1

2

if we can.

3

MR. OLAH: I will continue then.

4

THE COMMISSIONER: Yes, all right.

2-3

5

MR. OLAH: Q. Let us then turn

6

to the pathophysiologic causation that you posited
and, frankly, Doctor, I have some trouble under-

7

standing that explanation. Perhaps you could take

8

a moment and just lead me through it hand by hand.

9

A. Which aspect of it?

10

Q. Well, how is it that you

11

feel or can you explain how pathophysiologic

12

causation would have occurred in the case of Kevin
Pacsai?

13

A. That is a remarkably non-

14

specific question.

15

Q. Well, that just demonstrates

16

my sheer ignorance.

17

A. Well, okay. I mean, it is

18

almost impossible to answer. I mean, I am sure you

19

have heard at great length from Dr. Spielberg and

20

certainly from Dr. Bain and in somewhat briefer

21

length from me this morning what the possibilities
are. I mean, there is evidence certainly in Pacsai

22

that there was a primary metabolic disorder of some

23

kind. We have the evidence that he did have

24

25



2-4

1
2 an episode of acidosis in Hamilton, with really
3 quite profound acidosis that at the limits of
4 PH readings associated with the survival. He
5 certainly had hyperkalemia, although, as was pointed
6 out to me by Mr. Shinehoft, it wasn't quite as
7 striking as that that was seen here, but levels of
8 5.6 and 5.8 milli equivalence per litre are not
9 normal potassium readings. He then has high
10 potassium readings again at the Hospital for Sick
11 Children and, as it happens, those are associated
12 with high digoxin levels. But you are left with
13 a variety of possibilities. Either he has a
14 primary abnormality of potassium metabolism and
15 acid base metabolism which then leads to an ab-
16 normality of digoxin binding and causes displacement
17 of digoxin and a high, spuriously high digoxin
18 value, if you will, or else he has received - the
19 second possibility is that he has received an
20 overdose either intentional or inadvertently of
21 digoxin, and the third possibility is that there
22 is just something totally unique about Kevin
23 Pacsai in that he is unable for some reason to bind
24 digoxin in the normal fashion in his heart or
25 other tissues.

Q. Let's pause there for a



2-5

1

2

moment and let's deal with the last point. Is there any evidence pointing to that, any hard scientific evidence?

3

4

5

A. Only the high digoxin value in an otherwise unexplained fashion.

6

7

Q. All right. But other than that possibility there is no objective manifestation that would lead you to that conclusion?

8

9

A. No. And I will anticipate your next question, I am not aware of any literature that describes this as happening.

10

11

12

Q. That wasn't my next question.

13

14

A. Okay.

15

Q. As I understand the situation then, in Category 2, namely, Pathophysiological Causation of Death, you are saying it could be the potassium or digoxin and that was the very point that you made to Mr. Lamek that when you were reduced to that category it is your opinion that on a range of 75 to 25 that was digoxin?

16

17

18

19

20

A. That's correct.

21

22

Q. So that we have ruled out cardiac or have made it highly improbable that cardiac conduction was the causation of Kevin's

23

24

25



2-6

1

2

death, right?

3

A. Well, you accept that. I

4

mean, I really have some difficulty with that.

5

But we will accept it as Dr. Rowe's opinion that

6

cardiac conduction disturbance is not the cause of
death.

7

Q. All right.

8

A. Although, I would suggest

9

to you that it is the immediate cause of death in

10

this child, whether it was digoxin induced or

11

otherwise.

12

Q. Well, that is the mechanism

13

of death?

14

A. You are probably quoting him

15

out of context?

16

Q. That is the mechanism of

17

death, isn't it, Doctor?

18

A. Well ---

19

Q. Anyway, let's just go back

20

to then the other category and when we come to that

21

then, it is 75 per cent in your opinion digoxin and

22

only 25 per cent something pathophysiological?

23

A. That's right.

24

Q. Right. So that when we

25

tie all of that together, isn't it fair to say,



2-7 1
2 Doctor, that your present position in terms of
3 probability is that it is more probable than not
4 that Kevin Pacsai died of digoxin overdose?

5 A. Yes, I believe that is what
6 I stated very clearly this morning.

7 Q. And when you put it on some
8 sort of a spectrum it would be something in the
9 range of about 75 per cent certitude?

10 A. I would agree with that.

11 Q. Thank you.

12 Now, Doctor, I would like to deal
13 with the Lombardo child if I may. I know the problems
14 that you have as a scientist with exhumed tissue.
15 I was wondering if you could for a moment assist
16 me by turning to Exhibit 95C, which is the report
17 of the Centre of Forensic Sciences; in particular,
18 if you could turn to page ---

19 A. No, I am sorry, I don't
20 have that report.

21 Q. That's the report of March
22 25, 1982, Doctor.

23 A. I think I had them earlier.

24 MR. LAMEK: I can probably lend you
25 mine.

THE COMMISSIONER: I think one is



ANGUS, STONEHOUSE & CO. LTD
TORONTO, ONTARIO

MacLeod, cr.ex.
(Olah)

4459

2-8

1

2

coming from some place else.

3

MR. OLAH: Have we got it, Doctor?

4

THE WITNESS: No, I don't.

5

THE COMMISSIONER: Not yet.

6

MR. OLAH: Well, why don't I give you

7

mine.

8

9

10

11

12

13

14

15

16

17

18

19

20

21

22

23

24

25



DM.jc
JJ

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25

MR. OLAH: Well, why don't I give
you my copy?

MR. LAMEK: That is all right, I
will give the doctor mine. March 25?

MR. OLAH: That is correct, Mr. Lamek.

Q I was wondering if you could
look at Sample 60 and 61, 60 is on the very bottom
of that page and 61 is on the top of the next page.
You will see that there was apparently digoxin found
in the contents of the stomach and also in the small
bowel.

A. Yes.

Q Is there any conclusions that
you can draw, not from the levels, but from the fact
that in the contents of the bowel and the stomach
digoxin was found?

A. This body was exhumed after
nine months?

Q I think after almost a year,
Doctor.

A. Almost a year. No, I couldn't
draw any conclusion.

Q In your opinion, how would
digoxin get into the contents of the stomach and the
small bowel?



JJ.2

1

2

3

4

5

6

7

8

9

10

11

12

13

14

15

16

17

18

19

20

21

22

23

24

25

A. I don't know what the meaning of stomach contents is in a body that has been in the ground for nine months or a year. You know, I am surprised there is anything there that could be called stomach contents. You know, when one uses the term "stomach contents" you are usually referring to fluid in the stomach and bowel.

Q. Fluid or digested food.

A. Sure, it is there in life. Now, I mean, I can't think of any way that there would be anything other than desiccated tissue left in the stomach or bowel after this period of burial. Contents presumably refers to tissues that are scraped off the stomach wall, or scraped off the bowel wall and this is really no different from other tissues.

I mean, you can ask Mr. Cimbura what he means by that but I am sure that this is not stomach contents or bowel contents in the normal sense of the word.

THE COMMISSIONER: I don't think he was responsible for that, it is bearing the label "stomach", I don't think he put the label on it. I think it was put on by someone when it was given to him.

THE WITNESS: Yes. It is tissue, in



JJ.3

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25

fact it says "sample of tissue" and then it is reported as contents isolated from the stomach. Well, you know, tissue is not contents unless - maybe he is referring to some food particles that were left behind in the stomach, but I think that is pretty unlikely in a newborn baby. So to be honest I just can't think of any way that this can be interpreted.

Q. Fair enough, Doctor. Are you familiar with the reading found in the Belanger baby who was also exhumed?

A. Yes, I have seen the numbers at one time or another.

Q. It might be helpful for you to look at Exhibit 95E, which is the report of September 29th, 1982 on page 2. I would like you to look at the two together, because frankly what I was struck by was that in both cases - I am sorry, it is the bottom of page 3, you have got mass spec being used, and we know that there is digoxin found in children who were not on digoxin. But what I was struck by was that the readings in Lombardo seemed to be substantially higher than in Belanger. Perhaps I may be in error there, Doctor, because there was only two readings on Belanger. But if you have a look at liver it is 253, and liver in Lombardo is



JJ.4

1

2

354; and muscle is 43 in Belanger and muscle in
Lombardo is 218.

3

4

The question I have, Doctor, and it
may just relate to the different mode, one body was
embalmed and the other one was not. Is there any
assistance that you would draw from the higher levels
in the Lombardo child as opposed to the Belanger
child? What was the length

5

6

7

8

9

A. What was the length of
interment for Belanger?

10

11

Q. It was somewhat less, as I
recall it was probably about the same because they
both died the same, about the same time frame, I
think, Lombardo died a week or two later.

12

13

14

A. Again it really - I think it
would be very imprudent to try to interpret these
in any way. Clearly these concentrations reflect
an element of dehydration or desiccation, tissues
that may reflect post mortem bacterial colonization
of the body and destruction of digoxin by bacteria,
a completely unknown factor to us, and they also
reflect the fact as is evident in any of the post
mortem tissues studies that have been done that
there is a twentyfold variation in the kinds of
tissue concentrations that you achieve after a

15

16

17

18

19

20

21

22

23

24

25



JJ.5

1

2

3

4

5

6

7

8

9

10

11

12

13

14

15

16

17

18

19

20

21

22

23

24

25

standard dose. So, I mean, how could one expect to interpret these differences in post mortem tissues. In fact, it is this intrinsic uninterpretability of post mortem tissues that led us to believe that the police and the coroner should stop exhuming bodies, those results cannot be interpreted other than in a strictly qualitative sense as we have tried to do this morning.

Q. The only other question I have with respect to these kind of tissues and the ratings; is given the high levels that are found certainly in Lombardo, can you assist us as to whether an administration would have happened a very substantial period of time, or would you expect administration to have occurred a substantial time before death or closer to death? Assuming that there is an accidental administration of a fairly small amount would you not expect, Doctor, if it had occurred six days prior to death not to find levels of that magnitude?

A. I don't think you could draw that conclusion. We simply don't know what these concentrations mean. As concentrations, they really are uninterpretable. As a quantitative indicator of the presence of digoxin, given the riders that I have put on that by the specific assay method, I think



JJ.6

1

2

3

4

they can be taken as a good indication that there was some exposure to digoxin at some time prior to death. I can't go any further than that.

5

6

7

8

9

10

11

Q Then turning to the Hines child where you don't have exhumed tissue but you have fixed tissue, does that assist you, or can you draw any inference from that; you will see if you go to Exhibit 95A, starting at the bottom of page 6 and continuing on to page 7. Let us for example take T44 which is liver, and tissue was found to contain 240 nanograms of digoxin and/or digoxinlike substance.

12

13

14

MR. ROLAND: Mr. Olah has introduced his question on the fixed tissues and then he goes to T44 which is exhumed.

15

16

MR. OLAH: I am sorry, Mr. Roland is absolutely correct.

17

18

19

20

Q Let us go then to a fixed tissue, let us go to the heart. You will see Note 2, Doctor, and I don't know if you have had a chance to look at the calculations or find out how Mr. Cimbura arrived at the calculations.

21

22

23

24

25



10nov83
JJ2.1
DMra

1
2 It is Note 1 actually I should
3 be directing you to:

4 "From the data derived from T6
5 it is estimated that concentration
6 of digoxin in the heart before
7 it was fixed in the Klotz solution
8 was not less than 252 nanograms
9 per gram."

10 And the simple question I have
11 is, can you help us, given that reading, whether you
12 would expect to find that kind of level in the tissue
13 if administration had been sometime substantially
14 prior to death?

15 A. There just is no way of
16 answering your question. I think we have -- first
17 of all, there is very real reason to be skeptical
18 about Mr. Cimbura's calculation here. I simply don't
19 believe that he can make that calculation.

20 Secondly, even if it is absolutely
21 correct, we simply don't have the data which would
22 allow us to say anything about the time prior to
23 death when the drug was administered on that basis.
24 The main reason for that uncertainty is this extreme
25 variability that has been demonstrated in every study
that has looked at tissue concentration of digoxin
in relationship to dosage.

Q. The last question I have



JJ2.2

1

2

3

4

5

6

7

8

9

10

11

12

13

14

15

16

17

18

19

20

21

22

23

24

25

before sitting down and letting you go home for the day is the range of multiplier; that is, pre mortem or ante mortem, as opposed to post mortem levels. You said they range from 2 to 15 and the 15 came from Gary Murphy, the Gary Murphy situation.

Are there any other multipliers above 4 that you are aware of other than Murphy?

A. Oh, yes. There are many.

Do you want me to quote you chapter and verse? I think in Hastreiter's own paper -- perhaps you could put that question to him when he is here, but I think his most recent paper has multiples up to the order of 10. I am not sure that I have it here.

I must say, in fairness, the multiplier on Murphy is probably spurious and it is high mainly because we have an ante mortem level of 1.8, which was taken some time prior to death. So, it is kind of an artificial thing to say what the multiplier is.

In Hastreiter's paper, which I am sure you have in evidence, the American Journal of Cardiology, August of 1983 - and I am just looking down his list here. He has got --

MR. LAMEK: Mr. Commissioner, that



1
JJ2.32 paper is not yet marked in evidence. I confess I
3 have copies of it and it can be marked at any time.

4 MR. OLAH: Perhaps this might
5 be an appropriate time, Mr. Commissioner.

6 THE COMMISSIONER: I don't know
7 whether Mr. Lamek has them in his pocket.

8 MR. LAMEK: No, I don't.

9 THE WITNESS: I am just eyeballing
10 the data, but the highest multiplier that I see
11 there is 5, actually. There is no disagreement
12 the average in our own data is 3.8 and, certainly,
13 that is very close to the average in Hastreiter's
14 data. I think his comes out to 3.6, actually.

15 If I say 2 to 15, I am just
16 quoting the extreme of the range. Most of them
17 certainly will fall within 2.2 to 5.

18 MR. OLAH: Q. What I wanted to
19 clarify with you, doctor, is why you say that, in
20 these cases, we should be using a multiplier of,
21 say, 25 per cent; that is, .25 or .50, rather than 5.

22 A. I am not saying you should
23 be using any multiplier. I am really only attempting
24 to point out to you that we don't know what the
25 appropriate multiplier is.

MR. OLAH: Thank you, doctor. I



JJ2.42

am much obliged.

THE COMMISSIONER: Thank you.

Yes, Miss Forster.

MS. FORSTER: I gather, when I was out of the room, you indicated that, on Tuesday, the argument will be confined to notice. I just wanted to state for the record we are not taking a position with respect to that issue, so it is unlikely that we will be here.

THE COMMISSIONER: Oh. Well, we will miss you.

MR. TOBIAS: Just so that I know where I should be and when next week.

THE COMMISSIONER: Tuesday, ten o'clock, right here, if you want to come. If you don't want to come -- all I am going to do is render some judgments and I have often rendered very lonely judgments without anyone taking offence at all.

MR. TOBIAS: May I ask you then, other than--I take it from what Miss Forster has said, the argument on Tuesday will be confined to the notice only. Has there been a decision made at all with respect to when argument is likely to take place on the issue of the police report?



1

JJ2.52

THE COMMISSIONER: No.

3

MR. TOBIAS: Thank you, sir.

4

MR. SHANAHAN: Mr. Commissioner,
when should we be ready then to cross-examine this
doctor?

6

7

MR. LAMEK: Certainly not next
week because Dr. MacLeod is out of town. I will
speak to him about it and give counsel lots of
notice.

8

9

10

THE COMMISSIONER: We have
scheduled other witnesses from out of town for the
three following weeks, so it may be a long, long
time.

11

12

13

14

MR. SHANAHAN: I am indicating
that I will be very short.

15

16

THE COMMISSIONER: Well, what do
you mean by "very short"? One question?

17

MR. SHANAHAN: No.

18

THE COMMISSIONER: Well, all
right.

19

20

21

22

23

24

25



KK/DP/ak

1
2
3 MR. ROLAND: Mr. Commissioner, since
4 we may not be seeing you for a week, one other issue --

5 THE COMMISSIONER: You have an
6 opportunity to see me on Tuesday.

7 MR. ROLAND: The CDC report, I gather
8 from Mr. Lamek's schedule we are only three weeks
9 away from hearing from the authors. As I understood
10 it, that is about the time frame you were talking
11 about of releasing it before they testified. Since
12 we are not going to be here next week, that could be
13 as short as two weeks.

14 MR. LAMEK: I can assure my friend
15 that it will probably be more than four weeks. I
16 think we are looking at the middle of December,
17 frankly.

18 MR. ROLAND: I take it that we are
19 going to be getting it in the next week or two?

20 THE COMMISSIONER: No, my initial
21 idea was 10 days. With some counsel, it is not a
22 problem but I would think - every counsel now has
23 the expurgated copy which leaves out very small amounts,
24 so even 10 days I think was generous or it now has
25 become generous. It was not generous at the time.

MR. ROLAND: What is not in the
expurgated version is something that at least from my



1
2
3 client's perspective we would like at the earliest.
4 If 10 days is the limit, all right, but that needs
5 to be, it seems to me, analyzed by some experts,
6 whatever it says, before the testimony is given.

7 THE COMMISSIONER: I hate to have
8 more private meetings but would you mind having a
9 word with me in private after this is over? All
10 right.

11 MR. TOBIAS: Perhaps if Mr. Lamek
12 could just give us an outline of who he intends to
13 call the week we get back ---

14 THE COMMISSIONER: He intends to
15 call - he told us --

16 MR. LAMEK: My strong hope is that
17 it will be Dr. Hastreiter. I cannot confirm that
18 until I have spoken to him again, which I have to do
19 tomorrow. If it be not Dr. Hastreiter that week
20 I hope that perhaps Dr. MacLeod may be able to come
21 back to finish his evidence and we will have Dr. Fay
22 as well.

23 The week of the 28th, it has been
24 arranged that Dr. Kauffman will be here and my
25 expectation is that he will take all or at least the
better part of that week, and following that I think
we can expect to call Dr. Mirkin, or Dr. Hastreiter if

KK2



1
2 he does not come the week of November 21.

3 As soon as all these gentlemen have
4 been cleared out of the way, I propose to call the
5 authors of the Atlanta Report.

6 MS. KITELY: Mr. Commissioner, for
7 those of us who have not cross-examined this witness
8 yet, we need to know as soon as possible when he will
9 be back. Could counsel advise us tomorrow, perhaps?

10 THE COMMISSIONER: We won't know
11 that ---

12 MR. LAMEK: I'm sure Tuesday would
13 provide everyone with plenty of time. I'll let
14 people know on Tuesday.

15 THE COMMISSIONER: This is a
16 proposition that I find very strange because it
17 seems to me that there is no reason why you could
18 not prepare tonight or tomorrow morning between
19 2:00 and 4:00 if you wanted to.

20 MS. KITELY: Mr. Commissioner, it
21 is not the preparation. I have to make sure that
22 I can come back for it.

23 THE COMMISSIONER: Oh, that you can
24 be here. I beg your pardon. That is different.
25 We will try and sort that out. Yes.

MR. BROWN: With respect to Dr. Fay.



KK4

1

2

3

4

5

6

7

8

9

10

11

12

13

14

15

16

17

18

19

20

21

22

23

24

25

if indeed Dr. Fay testifies in two weeks time,
would it be possible for Commission Counsel to make
available to us Dr. Fay 's report in advance of his
being here to testify.

MR. LAMEK: There's no problem
with that. I will distribute it on Tuesday morning.

THE COMMISSIONER: Is there a report?

MR. LAMEK: Yes, well, there is a
summary, a few paragraphs prepared by Dr. Fay

THE COMMISSIONER: Anything else?

All right.

---Whereupon the hearing adjourned at 4:55 p.m. until
Tuesday, November 15th, 1983 at 10:00 a.m.

